Strategie di semplificazione a due farmaci per via orale

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DISCLOSURES

I have read and understood ICMJE policy on declaration of interest and I declare that in the past five years

- My institution has received research grants from AbbVie, Gilead Sciences, Bristol Myers Squibb, Janssen-Cilag and ViiV Healthcare

- I received speaker and consultancy honoraria from Gilead Sciences, Insmed, Janssen-Cilag, MSD, Roche, Sobi and ViiV Healthcare

EACS Guidelines 2022 – pazienti con SV

Indications

1. **Documented toxicity** caused by one or more of the antiretrovirals included in the regimen, see Adverse Effects of ARVs and Drug Classes
2. **Prevention of long-term toxicity**, see Adverse Effects of ARVs and Drug Classes. This may include person's concerns about safety
3. **Avoidance of drug-drug interactions,** page 26. This includes ART switch when starting HCV treatment to avoid DDIs, see Drug-drug Interactions between Viral Hepatitis Drugs and ARVs
4. **Planned pregnancy or women wishing to conceive,** see Treatment of Pregnant Women Living with HIV or Women Considering Pregnancy
5. **Ageing and/or comorbidity** with a possible negative impact of drug(s) in current regimen, e.g. on CVD risk, metabolic parameters
6. **Simplification**: to reduce pill burden, adjust food restrictions, improve adherence and reduce monitoring needs
7. **Protection from HBV** infection or reactivation by including tenofovir in the regimen
8. **Regimen fortification**: Increasing the barrier to resistance of a regimen in order to prevent VF (e.g. in persons with reduced adherence)
9. **Cost reduction:** switching to the generic form of their current regimen, if available

In persons with suppression of HIV-VL < 50 copies/mL for the past 6 months these dual therapy strategies should only be given if there is

a) no historical resistance and

b) HBV immunity or if non-immune concomitant HBV Vaccination

Dual therapies supported by large randomized clinical trials or meta-analyses:

DTG + RPV
XTC + DTG
XTC + DRV/b
Long-acting CAB + RPV bi-monthly injections

In clinical trials, these strategies have not been associated with more virological rebounds than triple therapy. There were a few cases of resistance development on DTG + RPV and CAB + RPV

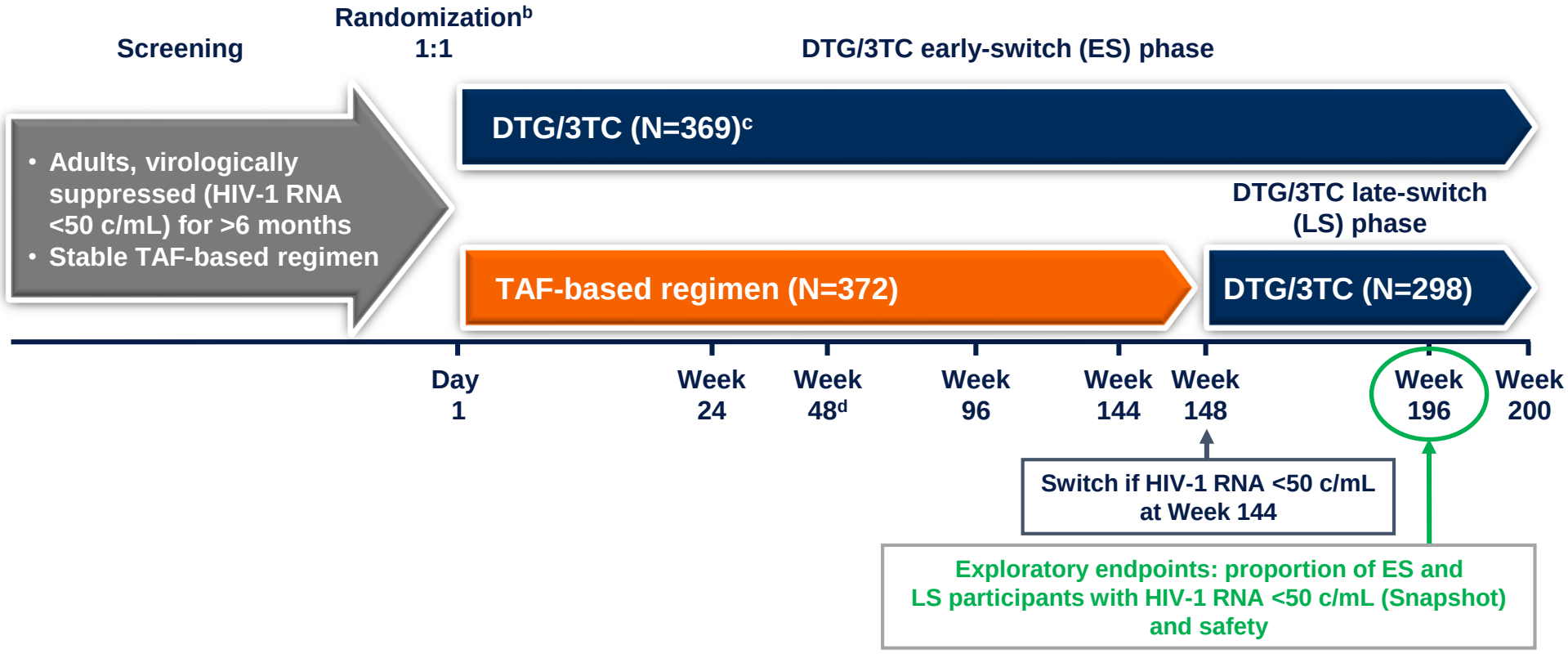
Dual therapy options supported only by small trials:
These regimens should be indicated only in persons not eligible for other treatment combinations due to intolerance or resistance to other drugs

DRV/b + RPV
DRV/b + DTG

TANGO Study Design

Phase 3 randomized, open-label, multicenter, parallel-group, non-inferiority study

Eligibility criteria
- ≥2 documented HIV-1 RNA measurements <50 c/mL
- No HBV infection or need for HCV therapy
- No prior virologic failure and no documented NRTI or INSTI resistance
- TAF/FTC + PI or INSTI or NNRTI as initial regimen[a]

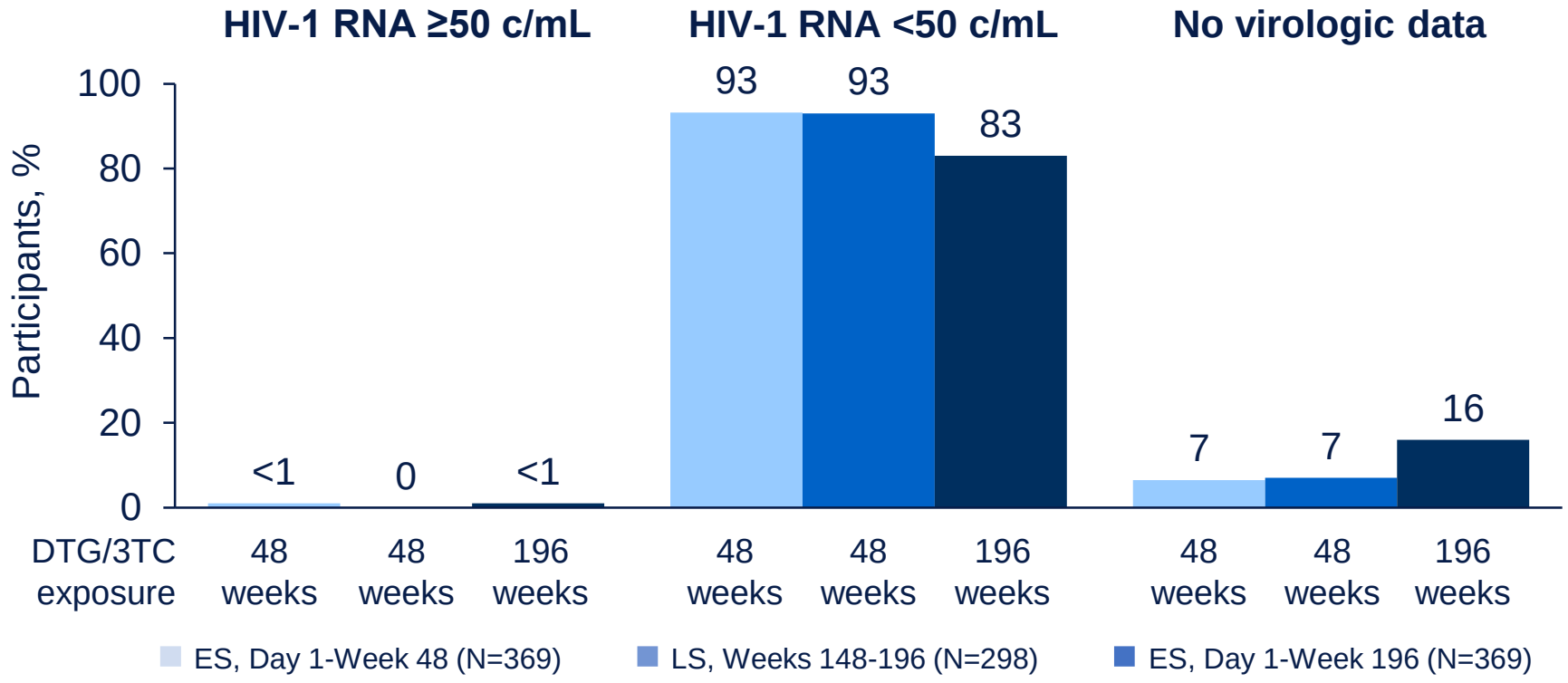


[a]Participants with initial TDF treatment who switched to TAF ≥3 months before screening, with no changes to other drugs in their regimen, were also eligible. [b]Stratified by baseline third agent class (PI, INSTI, or NNRTI). [c]2 participants excluded who were randomized but not exposed to study drug. [d]Primary endpoint was proportion of participants with plasma HIV-1 RNA ≥50 c/mL at Week 48 (Snapshot, ITT-E), with a 4% non-inferiority margin.

Smith et al. IAS 2023; Brisbane, Australia. Poster EPB0218.

Overall Efficacy Results at Week 196 (Snapshot, ITT-E Population)

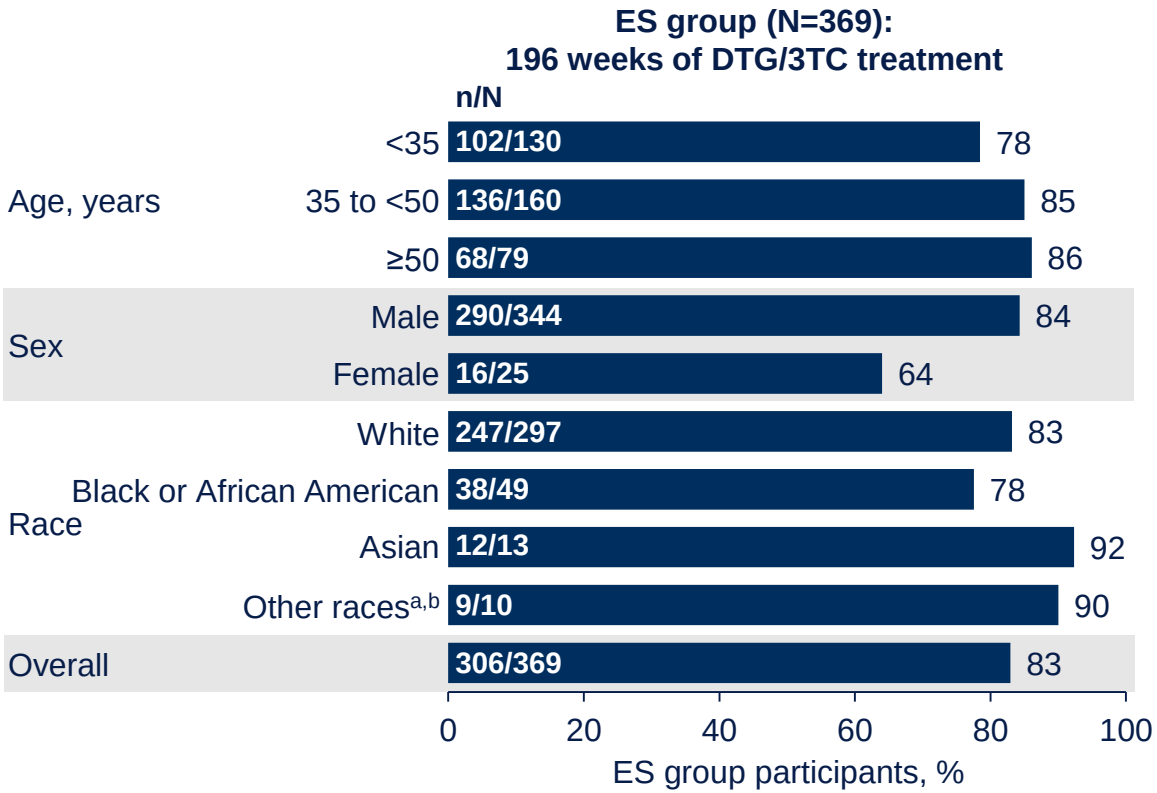
- Few ES participants (3/369 [<1%]; 95% CI, 0.0%-1.7%) and 0/298 (95% CI, 0.0%-0.0%) LS participants had HIV-1 RNA ≥50 c/mL in the overall population at Week 196 by Snapshot analysis (ITT-E)
- Confirmed virologic withdrawal criteria were met by 1/369 (<1%) ES participant and no LS participants through Week 196, with no resistance observed

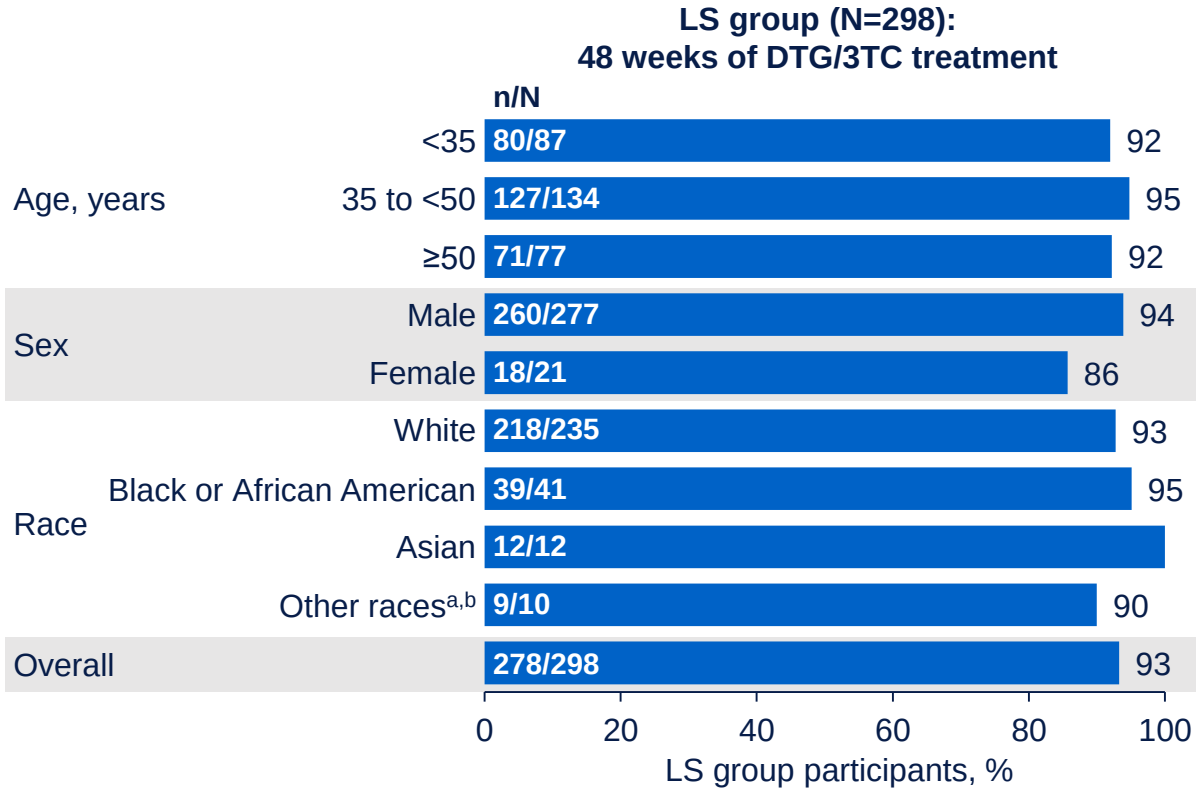


Smith et al. IAS 2023; Brisbane, Australia. Poster EPB0218.

Proportion of Participants in the ES and LS DTG/3TC Groups With HIV-1 RNA <50 c/mL at Week 196 Overall and by Demographic Subgroups (Snapshot, ITT-E Population)

- Overall ES group and LS group Snapshot virologic response rates at Week 196 were generally consistent with rates across their respective subgroups related to demographic characteristics



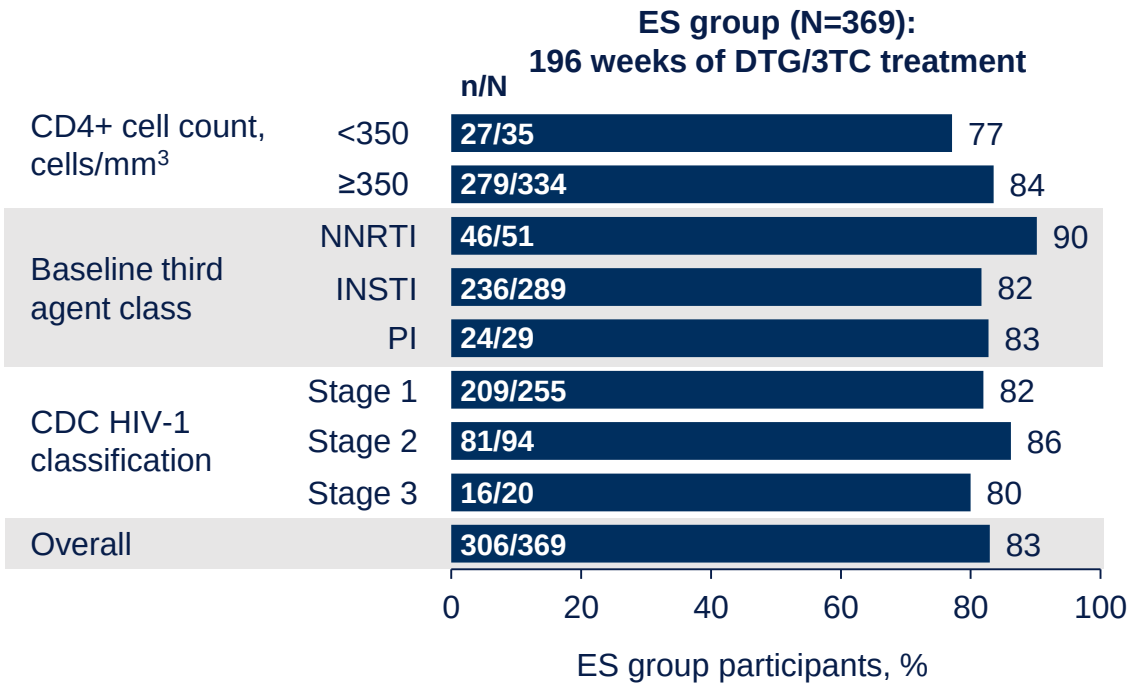


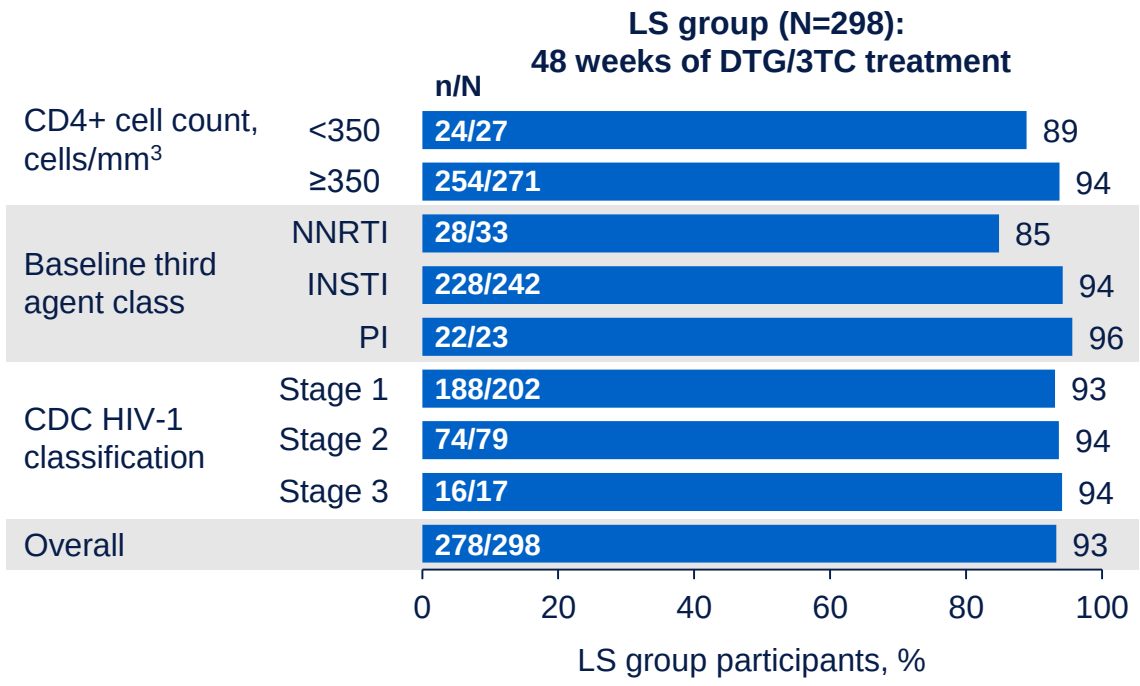
ES, early-switch (participants who switched to DTG/3TC on Day 1); LS, late-switch (participants who switched to DTG/3TC at Week 148). [a]Includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and individuals of multiple races. [b]After Week 144, an ES group participant initially categorized as Black or African American was reclassified as Other race by the investigational site.

Smith et al. IAS 2023; Brisbane, Australia. Poster EPB0218.

Proportion of Participants in the ES and LS DTG/3TC Groups With HIV-1 RNA <50 c/mL at Week 196 Overall and by Baseline Characteristics Subgroups (Snapshot, ITT-E Population)

- Overall ES group and LS group Snapshot virologic response rates at Week 196 were consistent with rates across their respective subgroups related to baseline disease characteristics and baseline third agent class at Week 196



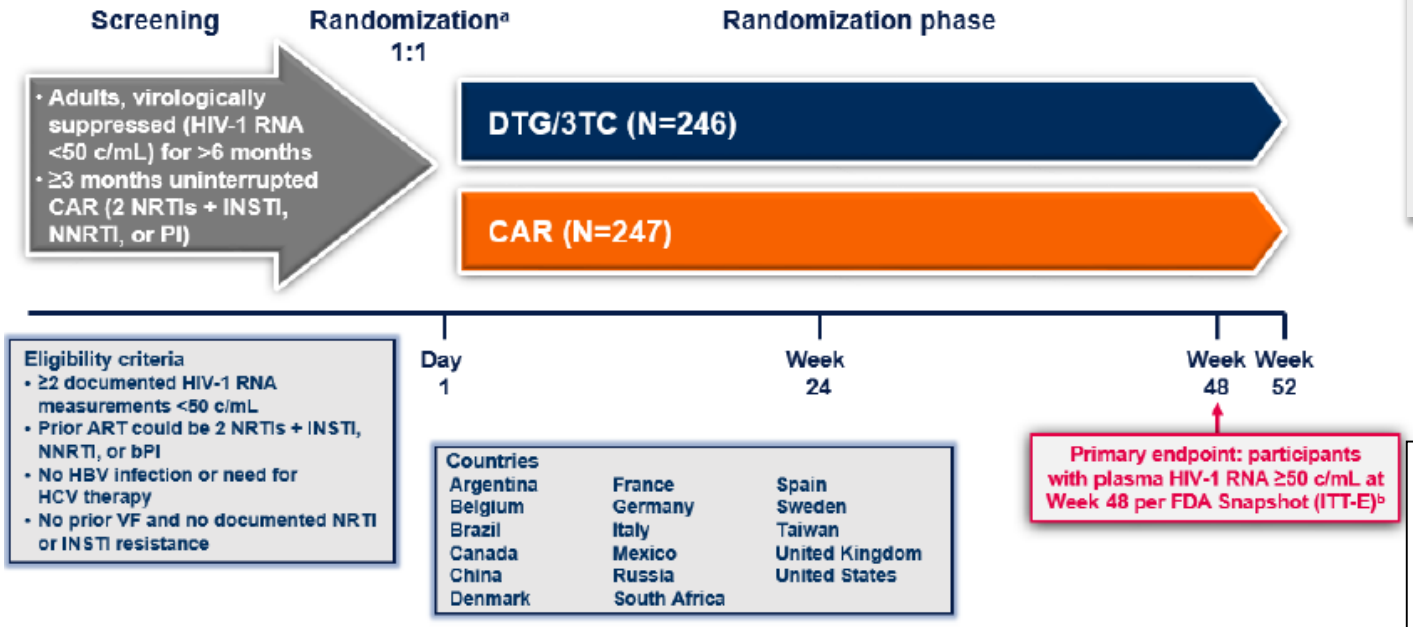


ES, early-switch (participants who switched to DTG/3TC on Day 1); LS, late-switch (participants who switched to DTG/3TC at Week 148).

Smith et al. IAS 2023; Brisbane, Australia. Poster EPB0218.

SALSA trial

Dolutegravir + lamivudine (DTG+3TC)



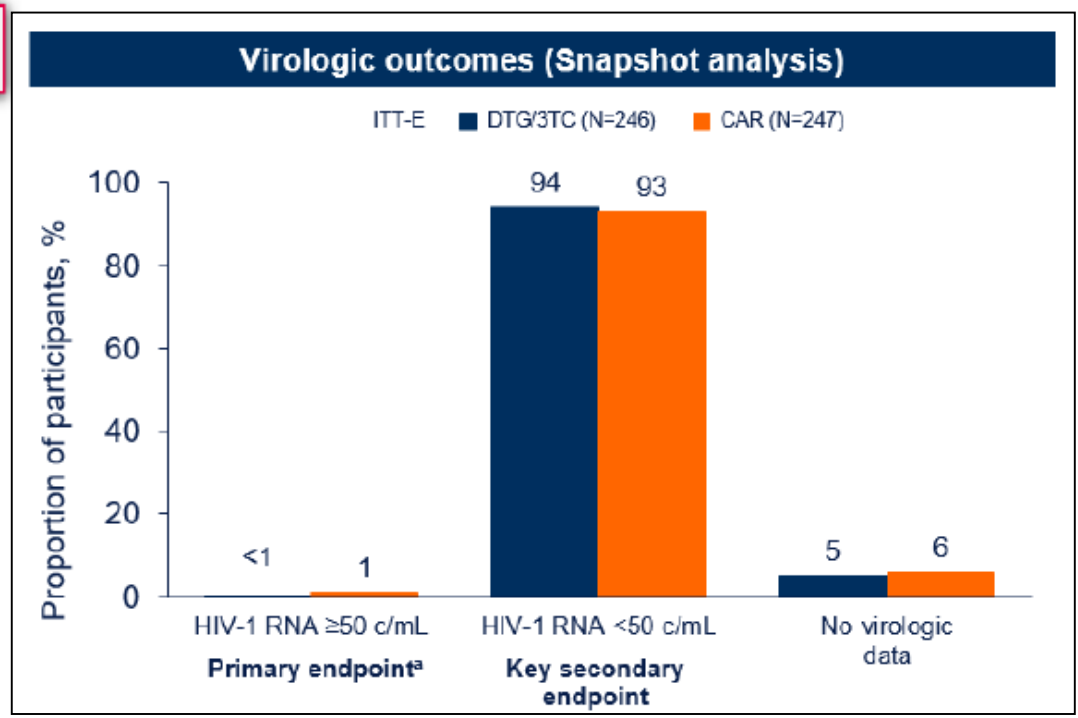
[a]Stratified by baseline third agent class (PI, INSTI, or NNRTI). [b]5% non-inferiority margin.

SALSA compared to **TANGO** trial:

- ✓ More women (~ 44-34 vs 7%)
- ✓ More non-white (~ 40 vs 23%)
- ✓ More > 50 years (~ 40 vs 20%)

No emergenceof resistance
(no one with CVW*)

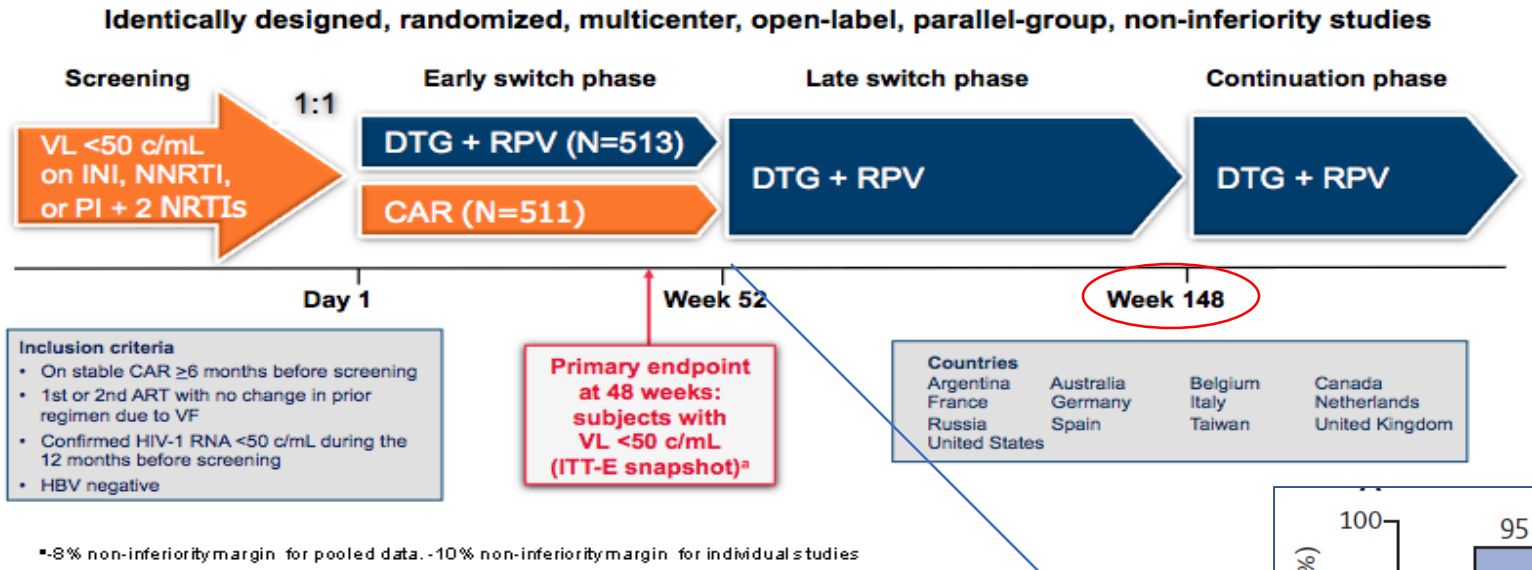
*CVW: confirmed virological withdrawal



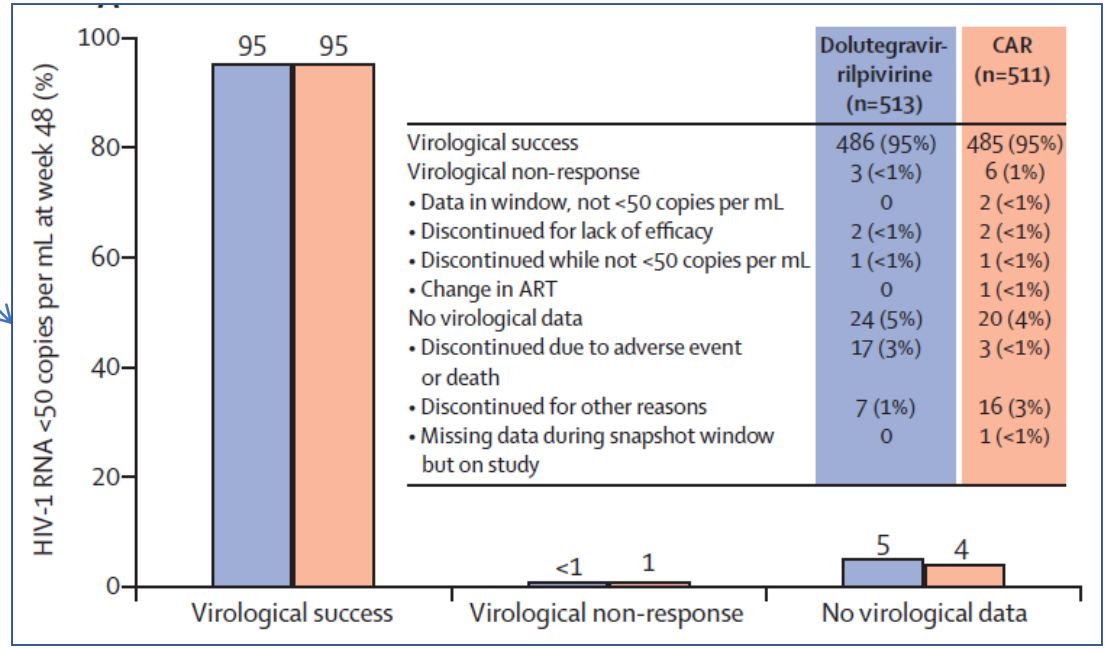
Llibre et al. IAS 2021; Virtual. Slides OALB0303

Dolutegravir + rilpivirine (DTG + RPV)

SWORD 1&2 trials



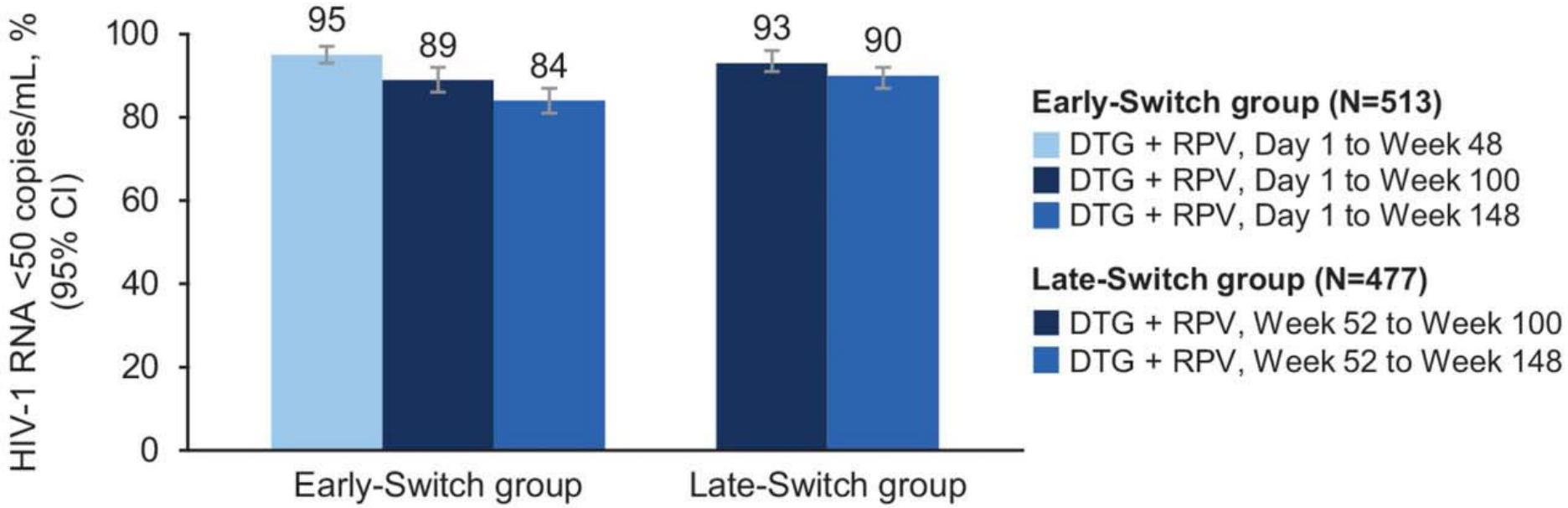
Entry criteria:
- no prior virologic failure
- no documented resistance mutations
- no HBV infection



	Dolutegravir-rilpivirine (n=513)	CAR (n=511)
Virological success	486 (95%)	485 (95%)
Virological non-response	3 (<1%)	6 (1%)
• Data in window, not <50 copies per mL	0	2 (<1%)
• Discontinued for lack of efficacy	2 (<1%)	2 (<1%)
• Discontinued while not <50 copies per mL	1 (<1%)	1 (<1%)
• Change in ART	0	1 (<1%)
No virological data	24 (5%)	20 (4%)
• Discontinued due to adverse event or death	17 (3%)	3 (<1%)
• Discontinued for other reasons	7 (1%)	16 (3%)
• Missing data during snapshot window but on study	0	1 (<1%)

Llibre JM, et al. Lancet. 2018;391:839-849

SWORD 1&2: virological efficacy at week 148



Emergence of resistance?

Van Wick J et al. JAIDS 2020;85;3

SWORD 1&2: resistance data at week 148

Virological failure in **11 pts** (1%): 8 in Early switch, 3 in Late switch

			Resistance mutations[a]				
			Baseline (GenoSure)[b]		CVW		
Week of failure	Previous regimen	Viral loads, copies/mL[c]	NNRTI	INSTI	NNRTI	INSTI	Fold change in sensitivity[d]
24	EFV/TDF/FTC	88; 466; 162	None	G193E	None	G193E	DTG, 1.02
36	EFV/TDF/FTC	1,059,771; 1018; <40	None	None	K101K/E	None	RPV, 0.75
64[e]	DTG/ABC/3TC	833; 1174; <40	None	N155N/H, G163G/R	None	V151V/I	—
76[e]	ATV, ABC/3TC	162; 217; 195	V108I	L74I	Assay failed		—
88	DTG/ABC/3TC	278; 2571; 55	None	None	E138E/A	None	RPV, 1.61 DTG, 0.72
88	RPV/TDF/FTC	147; 289; 503	Sample unavailable		K103N, V179I	None	RPV, 5.24
100	EFV/TDF/FTC	651; 1105; 300	K101E, E138A	G193E	K101E, E138A, M230M/L	Assay failed	RPV, 31
100	ATV, RTV, TDF/FTC	280; 225; 154	None	None	None	None	—
112	RAL/TDF/FTC	118; 230; 324	None	E157Q, G193E, T97T/A	M230M/L	E157Q, G193E	RPV, 2 DTG, 1.47
112	DRV, RTV, TDF/FTC	148; 219; 307	Viral load below assay cutoff		Viral load below assay cutoff		—
136[e]	EFV/TDF/FTC	4294; 7247; 40,020; 3378	Assay failed		E138A, L100L/I	Assay failed	RPV, 4.14

6/990 pts

48 weeks

100 weeks

149 weeks

Van Wick J et al.JAIDS 2020;85

TABLE 1 Characteristics of the patients included in the study.[a]

Variables	Values
Patients (n)	348
Male gender	237 (68.1)
Age (years)	54.0 (50.0–59.0)
HIV transmission category	
MSM	91 (26.1)
Heterosexual	83 (23.9)
IDU	149 (42.8)
Other	25 (7.1)
Years since HIV diagnosis	21.1 (14.7–25.4)
AIDS cases	116 (33.7)
Nadir CD4 count T cells/mm^3	160 (63–271)
Prior ART regimens ≥3	313 (90.5)
Prior virologic failure	179 (53.8)
Previous ART	
PI	110 (31.6)
NNRTI	71 (20.4)
INSTI	52 (14.9)
Other regimens	39 (11.2)
Reasons for starting DTG/RPV	
Convenience	151 (43.5)
Toxicity/intolerance	99 (28.4)
Drug interactions	59 (17.0)
Other	39 (11.2)

- 322 (92.5%) with virological suppression
- 26 (7.4%) without virological suppression
  (6 virological failure and 20 restarting ART)

10 cases had a detectable viral RNA load at 48 weeks (3 LTFU)

→ no emerging mutation

R. Palacios et al., HIV Med. 2023;24:933–937.

TABLE 2 Comparison of analytical parameters between baseline and 48 weeks after starting dolutegravir/rilpivirine.[a]

Variables	Baseline	48 Weeks	*P* value
Cholesterol (mg/dL)	193 (164–219)	181 (155–206)	0.0001
HDL-C (mg/dL)	45 (37–55)	47 (39–56)	0.9
LDL-C (mg/dL)	112 (90–136)	108 (84–129)	0.007
Triglycerides (mg/dL)	133 (96–187)	116 (85–158)	0.0001
Creatinine (mg/dL)	1.02 (0.7–1.0)	1.07 (0.8–1.1)	0.0001
eGFR (mg/mL/min)[b]	82.2 (73.1–91.0)	78.7 (66.6–90.0)	0.0001
GPT (IU/L)	27 (19–40)	25 (18–35)	0.002
GGT (IU/L)	34 (21–69)	27 (17–50)	0.0001
AP (IU/L)	80 (60–101)	69 (54–86)	0.0001

R. Palacios et al., HIV Med. 2023;24:933–937.

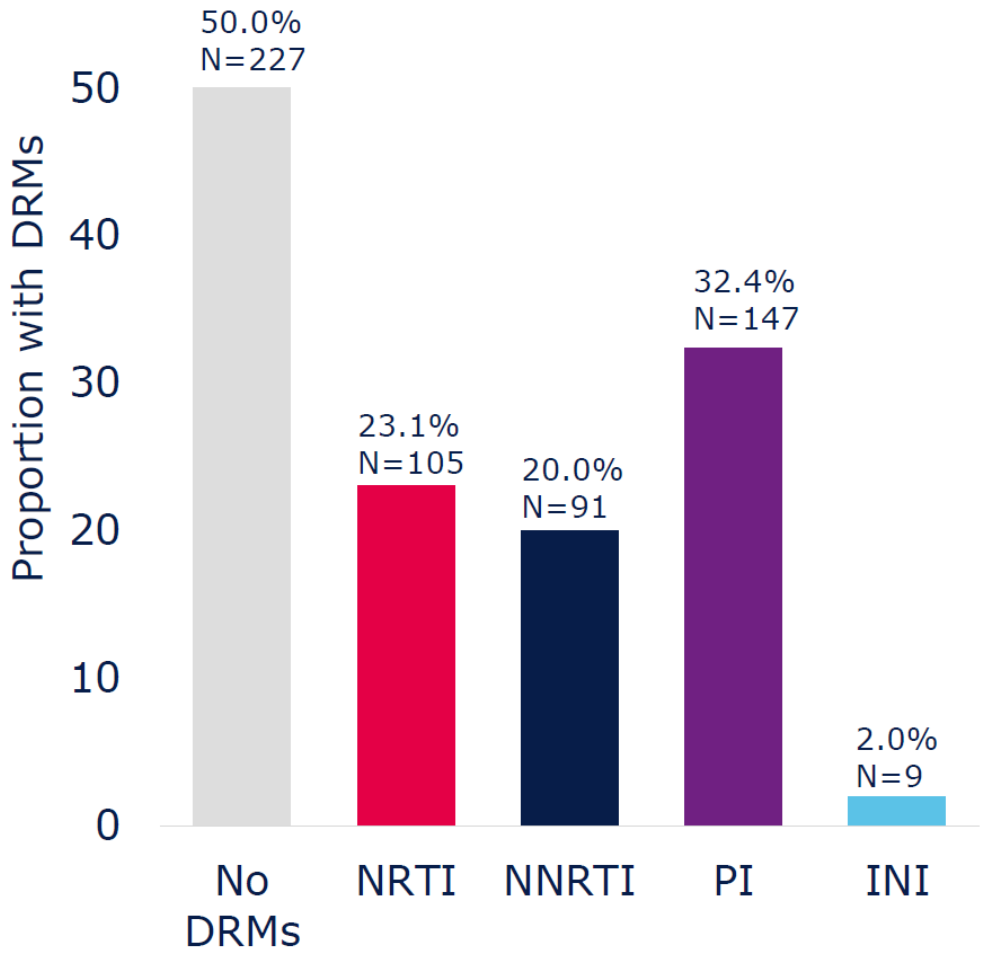
Baseline Characteristics

- A total of 735 individuals suppress-switched to an INI+RTI 2-DR
  - 534 (73%) dolutegravir (DTG)+lamivudine (3TC)
  - 186 (25%) DTG+rilpivirine (RPV)
  - 15 (2%) other INI+RTI 2-DR
- The 5 most common regimens individuals were being switched from were:
  - DTG+ABC+3TC - 134 (18.2%)
  - DTG+TAF+FTC - 50 (6.8%)
  - DTG+TDF+FTC - 42 (5.7%)
  - EFV+TDF+FTC - 36 (4.9%)
  - EVG/c+TAF+FTC - 31 (4.2%)

	Suppressed switch N=735
Age, years, median (IQR)	54 (47-59)
Gender, n (%): Male	556 (75.7)
Ethnicity, n (%):	
White	492 (66.9)
Black	140 (19)
Other	8 (1.1)
Unknown	95 (12.9)
Duration of antiretroviral treatment (years): median (IQR)	10.2 (4.7-18.8)
CD4 count nadir (cells/mm³): median (IQR)	250.5 (134-365)
CD4 count baseline count (cells/mm³): median (IQR)	684 (534-920)
Comorbidities, n(%):	
Hypertension	177 (24.1)
Hyperlipidemia	190 (25.9)
Renal disorder	102 (13.9)
Liver disorder	60 (8.2)
Diabetes	46 (6.3)

Mussini et al. IAS 2023; Brisbane, Australia. Poster EPB0209.

Drug Resistance Mutations by ART Class



- 454 (61.8%) individuals suppressed switching to a 2-DR had ≥ 1 documented resistance test at any point prior to baseline (38.2% had no resistance test results)
- Of those tested, 50.0% had documented resistance mutations in at least one class of ARVs

DRMs, Drug resistance mutations.
Resistance to a class of ART drugs indicated by presence of ≥1 mutation conferring reduced susceptibility to any drug within that class; resistance testing data were abstract from medical records.

Mussini et al. IAS 2023; Brisbane, Australia. Poster EPB0209.

Virologic Failure

- Among the 5 individuals who experienced a VF event on DTG+3TC, no one had a documented history of INSTI- or NRTI-associated resistance mutations
- Among the 5 individuals who experienced VF on DTG+RPV, 2 had history of NNRTI-associated resistance mutations (neither had mutations associated with reduced susceptibility to RPV) and no one had a history of INST-associated mutations
- Six VF events were identified by having a single VL ≥50 copies/mL at week 96, which was the end of study follow-up. Individuals may have resuppressed on their 2 DRs after follow up ended, but these outcomes were unobserved
- A sensitivity analysis using a threshold of VL≥200 copies/mL to define VF (using all component definitions) identified 3 VF events (KM estimate: 0.5% [95% CI: 0.2-1.5%])

	Events (N)	% (95% CI)
Kaplan-Meier estimate of VF Week 96 (by any definition component)	**10**	**1.6 (0.9 – 3.0)**
By individual VF definition component:		
Two consecutive VL≥50 copies/mL	1	0.1 (0.0 – 1.0)
One VL≥50 copies/mL followed by 2-DR discontinuation	3	0.4 (0.1 – 1.4)
1 VL ≥50 copies/mL and no follow-up values thereafter	6	1.1 (0.5 – 2.3)

Mussini et al. IAS 2023; Brisbane, Australia. Poster EPB0209.

Viral Load Measurements at 96 weeks

- There were 23 measurements of low-level viremia occurring over 1340 person-years of follow-up; incidence rate: 1.7 events per 100 person-years (95% CI: 1.1-2.6). 7 of 10 VF events were low level viremia
- There were 4 measurements of high-level viremia (VL ≥200 copies/mL), occurring over 1340 person-years of follow-up incidence rate: 0.3 events per 100 person-years (95% CI: 0.1-0.8)
  3 of 10 VF events were high-level viremia
- No resistance tests to identify emergent resistance mutations following VF or viral blip events were documented in the medical records

	Weeks 0-24	Weeks 24-48	Weeks 48-72	Weeks 72-96	Overall 0-96 weeks
N of participants	735	712	668	574	**735**
Number of VL≥50 copies/mL	7	9	4	7	**27**
Person-years of follow-up	364	356	334	287	**1340**
Incidence rate per 100 p-y	1.9	2.5	1.2	2.4	**2.0**
95% confidence interval of IR	0.8-4.0	1.2-4.8	0.3-3.1	1.0-5.0	**1.3 – 2.9**

*Includes VF events from virologic failure table plus viral blips.

Mussini et al. IAS 2023; Brisbane, Australia. Poster EPB0209.

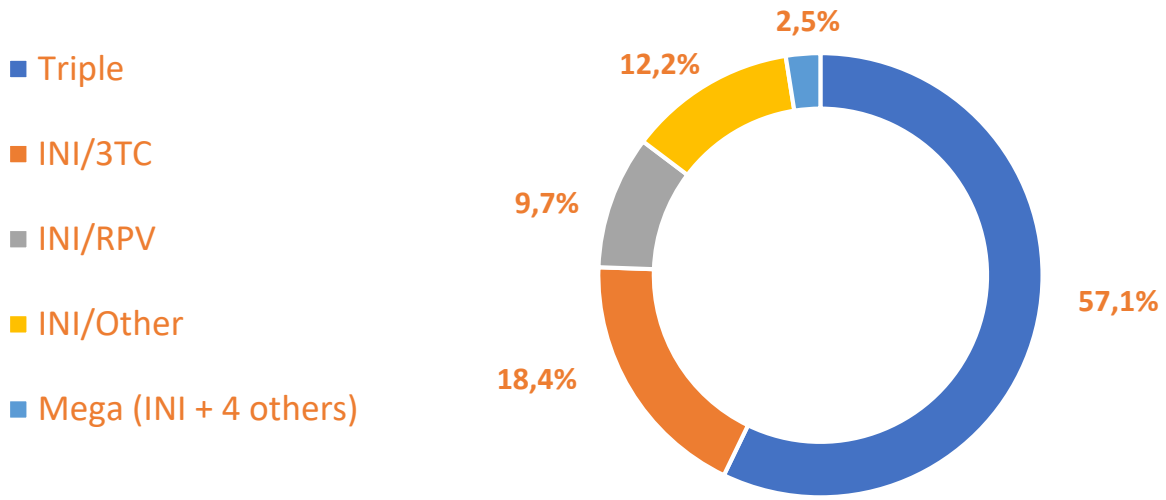
Dual regimens are often used in older PLHIV (OPLWH) in Italy

- Despite deprescribing becoming more common in geriatric medicine, data on dual ART therapies in EPLWH are limited[1]

Multi-centre **GEPPO (Geriatric Patients Living with HIV/AIDS) Italian cohort**[1,2]

- A cross-sectional analysis in 2019 included 882 OPLW receiving INI-based regimens[2]
  - Median age: 69.8 years; good immunovirological profile; multimorbidity present in 42.3% and polypharmacy in 27.4% of participants

40.3% of study participants were receiving dual therapies[2] (an increase from 25.4% in 2016[1])



Higher durability of DTG-containing regimens, with no difference among dual therapies between DTG and RAL[2]

1. Nozza S, et al. J Antimicrob Chemot 2017;72:2879–86
2. Focà E, et al. PlosOne 2021;16:e0258533

Article

Efficacy and Safety of Two-Drug Regimens with Dolutegravir plus Rilpivirine or Lamivudine in HIV-1 Virologically Suppressed People Living with HIV

Carlos Dueñas-Gutiérrez [1,*], Luis Buzón [2], Roberto Pedrero-Tomé [3], José A. Iribarren [4], Ignacio De los Santos [5], Sara De la Fuente [6], Guillermo Pousada [7], Miguel Angel Moran [8], Estela Moreno [9], Eva Ferreira [10], Julia Gómez [11] and Jesús Troya [12]

Rate of virological suppression at weeks 24, 48 and 96

	Overall		DTG/3TC		DTG/RPV		
	N	%	N	%	N	%	*p*-Value
ALL POPULATION							
24 weeks < 50 copies/mL	1357/1400	96.9	840/860	97.7	517/540	95.7	0.041
48 weeks < 50 copies/mL	1126/1156	97.4	697/711	98.0	429/445	96.4	0.091
96 weeks < 50 copies/mL	552/557	99.1	401/404	99.3	151/153	98.7	0.528
Non-AIDS POPULATION							
24 weeks < 50 copies/mL	887/913	97.2	497/511	97.3	390/402	97.0	0.825
48 weeks < 50 copies/mL	692/710	97.5	366/376	97.3	326/334	97.6	0.823
96 weeks < 50 copies/mL	221/223	99.1	119/121	98.3	102/102	100.0	0.192
AIDS POPULATION							
24 weeks < 50 copies/mL	216/230	93.9	95/98	96.9	121/132	91.7	0.098
48 weeks < 50 copies/mL	177/188	94.1	76/79	96.2	101/109	92.7	0.307
96 weeks < 50 copies/mL	89/89	96.6	38/39	97.4	48/50	96.0	0.710

Viruses 2023, 15, 936

Dolutegravir-based dual maintenance regimens combined with lamivudine/emtricitabine or rilpivirine: risk of virological failure in a real-life setting

Dat'AIDS cohort study

Variable	Dolutegravir/ rilpivirine, *N* = 799	Dolutegravir/xTC, *N* = 575
Virological failure, *n* (%)	30 (3.8)	15 (2.6)
one plasma HIV RNA value >400 copies/mL, *n* (%)	18 (2.3)	12 (2.1)
followed by discontinuation of dolutegravir-based maintenance dual therapy	8 (1.0)	5 (0.8)
two consecutive plasma HIV RNA values >50 copies/mL, *n* (%)	12 (1.5)	3 (0.5)
followed by discontinuation of dolutegravir-based maintenance dual therapy	9 (1.1)	1 (0.2)
time between two consecutive plasma HIV RNA values >50 copies/mL (days), median (IQR)	31 (18–54)	35 (21–74)
Dual therapy discontinuation, *n* (%)	170 (21.3)	104 (18.1)
time to discontinuation (months), median (IQR)	9.6 (4.2–19)	9.6 (3.6–18.7)
virological failure leading to discontinuation, *n* (%)	17 (2.1)	6 (1)
adverse event, *n* (%)	80 (10)	47 (8.2)
CNS symptom, *n* (%)	31 (3.9)	19 (3.3)
gastrointestinal disturbance, *n* (%)	7 (0.9)	8 (1.4)
cutaneous event, *n* (%)	5 (0.6)	2 (0.3)
arthralgia, *n* (%)	3 (0.4)	3 (0.5)
renal impairment, *n* (%)	3 (0.4)	2 (0.3)
dyslipidaemia, *n* (%)	1 (0.1)	0 (0)
other adverse event, *n* (%)	30 (3.8)	13 (2.3)
miscellaneous, *n* (%)	73 (9.1)	51 (8.9)
death, *n* (%)	12 (1.5)	9 (1.6)
drug–drug interaction, *n* (%)	7 (0.9)	2 (0.3)
other, *n* (%)	54 (6.8)	40 (7)

Deschanvres C et al. J Antimicrob Chemother. 2021, Oct 15

Dolutegravir-based dual maintenance regimens combined with lamivudine/emtricitabine or rilpivirine: risk of virological failure in a real-life setting

Dat'AIDS cohort study

Previous virological failure: 43.8% and 19.8% for DTG/RPV and DTG/XTC group, respectively.
More than 5 lines of therapy: 58.7% and 37.6%, for DTG/RPV and DTG/XTC group, respectively.

2D-Regimen	Number	Follow Up months	Virolog. Failure (%)	Discontinuation for VF	New resistance at failure
DTG+ xTC	575	19 (IQR: 11-31)	15 (2.6%)	6/15	0
DTG+ RPV	799	20 (IQR: 11-31)	30 (3.8%)	17/30	2

Table 3. Description of genotypes at virological failure with NRTI-, NNRTI- or INSTI-associated resistance mutations

					Resistance mutations			
					historical genotype		genotype at VF	
n	Second regimen	Time to VF	History of VF	Plasma HIV RNA at VF (copies/mL)	NRTI or NNRTI	INSTI	NRTI or NNRTI	INSTI
1	rilpivirine	W75	NNRTI	68, 133	K103H/N/S/T	none	K103H/N/S/T	none
2	rilpivirine	W6	no	531	none	none	E138K	none
3	rilpivirine	W32	no	142, 189[a]	none	none	K101E, E138K	N155H
4	rilpivirine	W86	no	474	not available	none	E138A	none
5	rilpivirine	W34	no	52 310	E138K	none	E138A, L100I	L74I[c]
6	rilpivirine	W5	no	109, 109	K103H/N/S/T	none	K103H/N/S/T	none
7	xTC	W29	NRTI	66, 59[b]	M184V	none	M184V	none

Deschanvres C et al. J Antimicrob Chemother. 2021;15

Dolutegravir-based dual maintenance regimens combined with lamivudine/emtricitabine or rilpivirine: risk of virological failure in a real-life setting

Colin Deschanvres [1]*, Jacques Reynes[2,3], Isabelle Lamaury[4], David Rey[5], Romain Palich [6], Firouzé Bani-Sadr[7], Olivier Robineau[8], Claudine Duvivier[9], Laurent Hocqueloux [10], Lise Cuzin [11,12], Veronique Joly[13], Francois Raffi[1], André Cabie[12] and Clotilde Allavena[1] on behalf of the Dat'AIDS Study Group†

Factors associated with dolutegravir-based maintenance dual therapy virological failures on dolutegravir/rilpivirine

	No virological failure, $N = 769$	Virological failure, $N = 30$	Univariate analysis		Multivariate analysis	
			crude HR	*P*	adjusted HR	*P*
Age (years), *n* (%)						
≤50	547 (71.1)	16 (53.3)	2.27 (1.1–4.76)	0.03	2.13 (0.98–5.26)	0.06
Gender, *n* (%)						
female	233 (30.3)	14 (46.7)	2.02 (0.99–4.14)	0.06	1.84 (0.77–4.45)	0.17
CDC stage, *n* (%)						
C	223 (29.0)	8 (26.7)	0.9 (0.4–2.03)	0.80		
Exposure, *n* (%)						
MSM	288 (37.5)	7 (23.3)	0.52 (0.22–1.21)	0.13	0.74 (0.26–2.1)	0.57
Nadir CD4 cell count (cells/mm^3), *n* (%)						
≤200	386 (50.2)	15 (50.0)	0.98 (0.48–2)	0.95		
Zenith plasma HIV RNA ($\log_{10}$ copies/mL), *n* (%)						
>5	368 (47.9)	20 (66.7)	2.01 (0.94–4.3)	0.07	1.88 (0.87–4.1)	0.11
Duration of viral suppression (months), *n* (%)						
≤12	46 (6.0)	4 (13.3)	2.41 (0.84–6.93)	0.10	2.35 (0.81–6.81)	0.12
Previous virological failure, *n* (%)						
regardless of the regimen	333 (43.3)	17 (56.7)	1.64 (0.79–3.4)	0.18		
under NRTI regimen	318 (41.4)	15 (50.0)	1.39 (0.67–2.85)	0.38		
under NNRTI regimen	81 (10.5)	9 (30.0)	3.37 (1.54–7.39)	0.002	2.97 (1.28–6.93)	0.02
under INSTI regimen	34 (4.4)	4 (13.3)	2.95 (1.02–8.56)	0.04	1.66 (0.47–5.80)	0.42
Start of first ART regimen, *n* (%)						
≤1996	196 (25.5)	6 (20.0)	0.7 (0.28–1.72)	0.44		

J Antimicrob Chemother 2022; **77**: 196–204

VF and RAMs at 1st or 2nd failure - VIROSTAR

Regimi	B/F/TAF n=2141	DTG/ABC/3TC n=1432	DTG+3TC n=452	DTG+RPV* n=298
Patients with VF	7%, n=150	8.1%, n=117	6%, n=27	5%, n=15
Emerging RAMS with VF	**4.7%, n=7**	**7.7%, n=9**	**18.5%, n=5**	**40%, n=6**
Emerging RAMS to INSTIs	1.3%, n=2 1 E138 1 Y143C	1.7%, n=2 1 G140S+Q148H 1 E92Q	3.7%, n=1 1 N155H	0%, n=0
Emerging RAMS to NRTIs	2.5%, n=5 5 M184V	6%, n=7 6 M184V 1 M184I	14.8%, n=4 4 M184V	N/A
Emerging RAMS to NNRTIs	N/A	N/A	N/A	40%, n=6 3 E138A 1 M230L 1 K101E 1 Y181C

Marcelin AG,e t al. Glasgow 2022.P225

Simmetria farmacologica

EMIVITA	PLASMATICA	INTRACELLULARE
ABC	1,5 ore	12-26 ore
3TC (FTC)	5-7 ore (10 ore)	18-22 ore (>20 ore)
TDF (TAF)	17 ore (0,5 ore)	>60 ore (150-180 ore)
EFV	40-55 ore	
DOR	15 ore	
RPV os (RPV LA)	50 ore (13-28 settimane)	
DRVr (DRVc)	15 ore (7 ore)	
BIC	~17 ore	
DTG	~14 ore	
CAB os (CAB LA)	41 ore (6-12 settimane)	

Source: DHHS Guidelines, Last Update Jan 20th 2022

PK of DTG/RPV?

virological replication was more frequent in PLWHA with subtherapeutic plasma concentrations, when using concentration thresholds of 640 ng/mL for DTG and 50 ng/mL for RPV.

TABLE 1 Baseline demographics, biological and treatment parameters of people living with HIV/AIDS.

	Median	IQR25–75%
Age (years)	56.0	51.0–63.0
Sex ratio (F/M)	0.37	
Weight (kg)	73.0	63.0–82.0
BMI (kg/m^2)	24.0	21.8–26.9
Nadir CD4 (cell/mm^3)	197	96–335
Zenith VL (cp/mL)	90 518	27 042-296 500
CD4/CD8 ratio	0.92	0.64–1.34
Reason for DTG/RPV dual therapy (*n*)		
Simplification	145	
Toxicity prevention	19	
Lipodystrophy	11	
Renal toxicity	12	
Other toxicity	16	
Treatment failure	6	

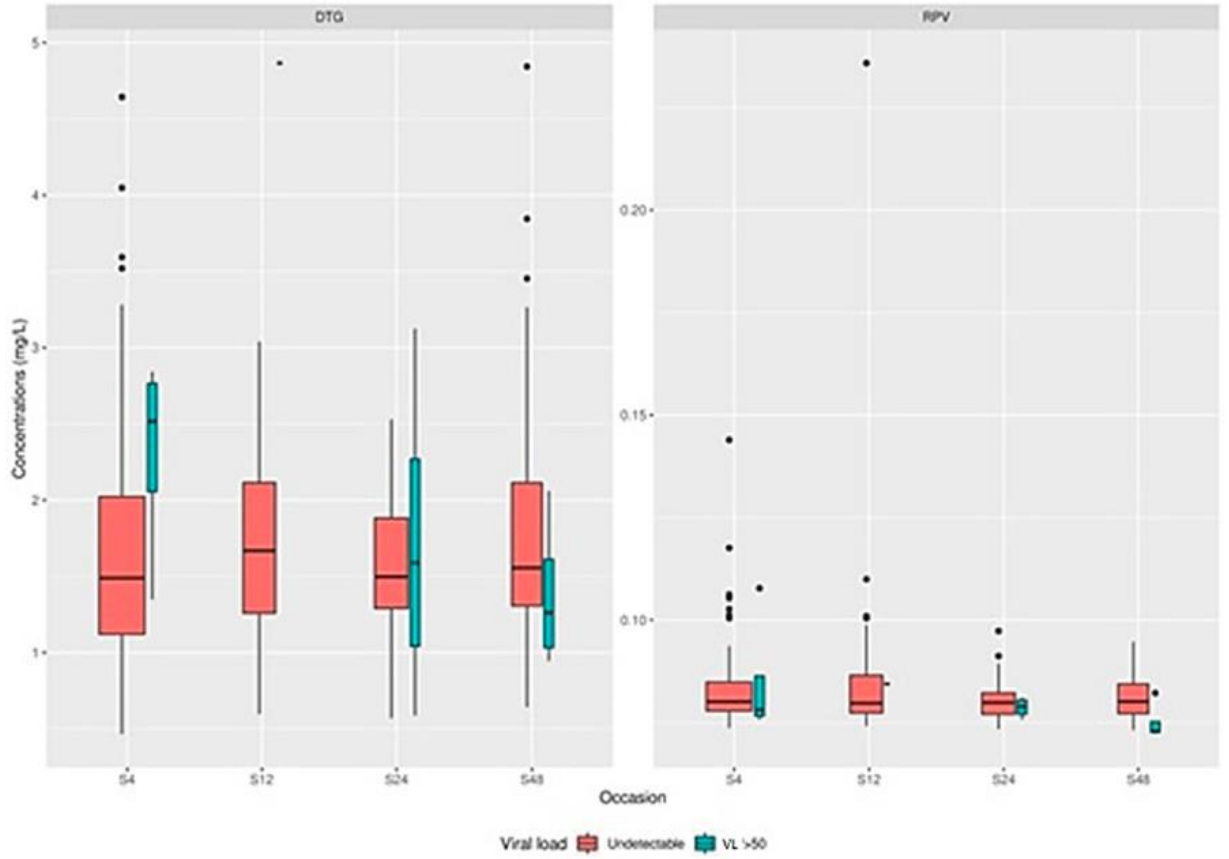
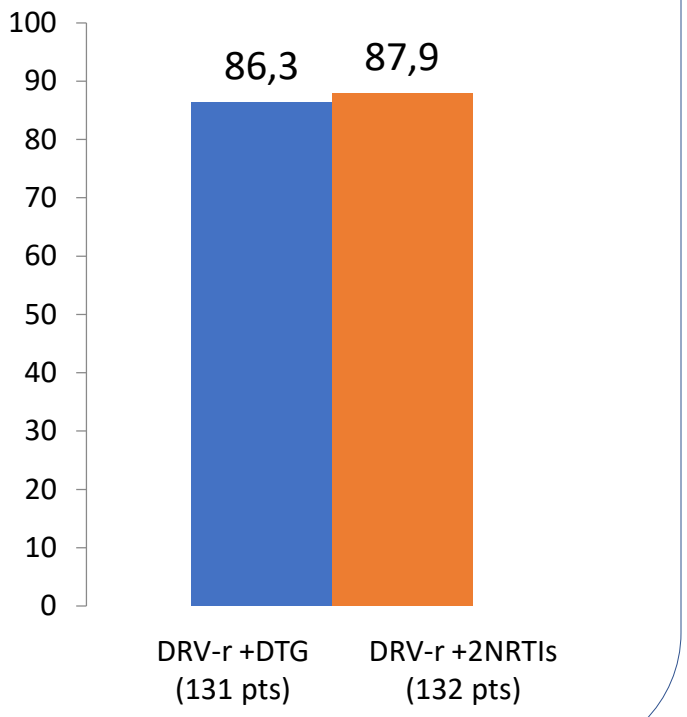


FIGURE 2 Relationship between predicted dolutegravir (DTG) and rilpivirine (RPV) trough concentrations and the occurrence of viral replication. VL, viral load.

LEMAITRE ET AL. Br J Clin Pharmacol. 2023;1–10.

Darunavir-r + DTG

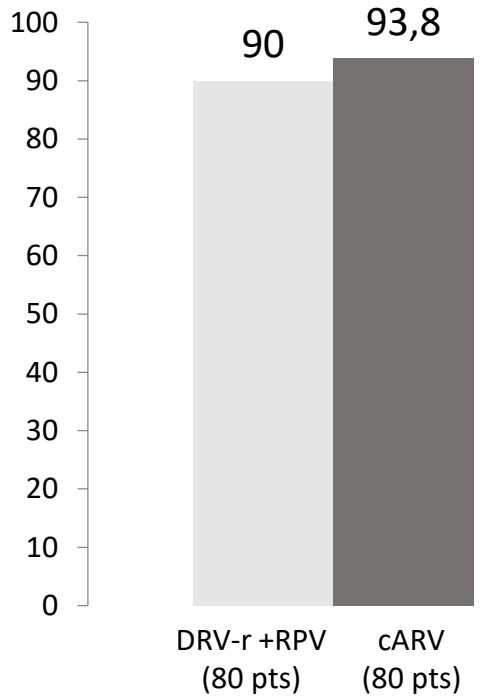
48-week data, randomized, switch trial (DUALIS), HIV RNA < 50 c/ml



No emergence of resistance

Darunavir-r + RPV

24-week data, randomized, switch trial (PROBE-2), HIV RNA < 50 c/ml



Spinner CD et al. Open Forum Infect Dis 2020;7:ofaa356

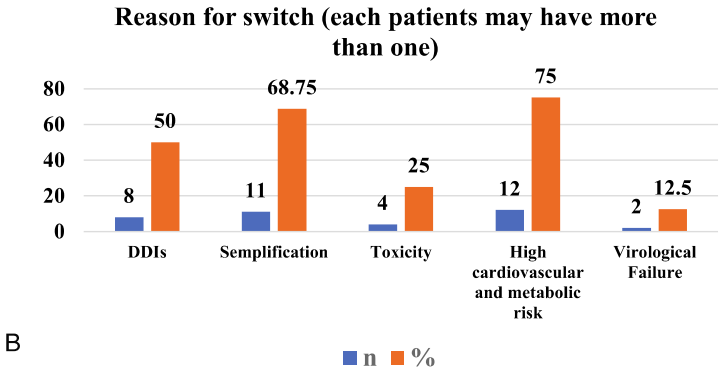
Maggiolo F et al. J Antimicrob Chemother. 2020;75:1332-1337.

Dolutegravir plus Doravirine DT

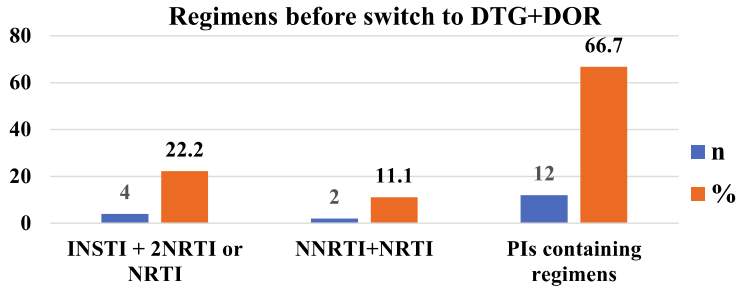
A

Comorbidity *each patient had more than 1	Overall 18 n (%)
Dyslipidaemia	16 (88.8)
Hypertension	14 (77.7)
Depression	7 (38.9)
COPD	6 (33.3)
Diabetes	5 (27.8)
Osteoporosis	5 (27.8)
Obesity	3 (16.7)
Cirrhosis	2 (1.1)
Ischaemic heart disease	2 (1.1)

B



C

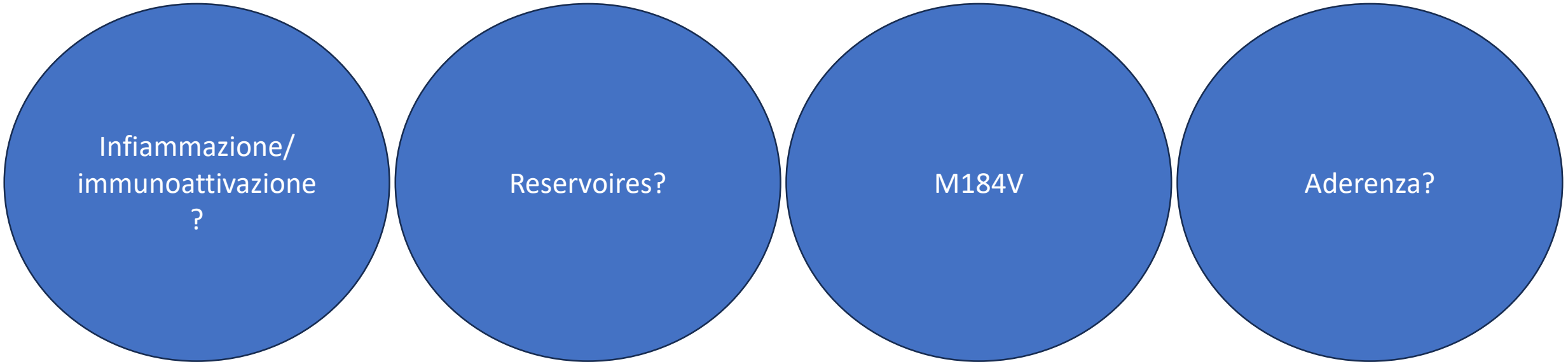


D

Parameter	Before switch, n(%)	After switch n (%)	p value
Undetectable HIV-RNA (Yes)	15 (88.2)	17 (100)	-
CD4+, cell/mm^3, mean (SD)	607 (240)	629 (232)	0.37
Cholesterol, mmol/L, mean (SD)	5.1 (3.3)	4.8 (1.4)	0.1
HDL, mmol/L, mean (SD)	1.5 (0.7)	1.1 (0.4)	0.75
LDL, mmol/L, mean (SD)	3.1 (1)	2.9 (1.1)	0.49
Triglycerides, mmol/L, mean (SD)	1.41 (0.7)	1.5 (0.7)	0.2
Fasting glucose, mmol/L, mean (SD)	6.2 (1.7)	5.5 (1.4)	0.08
BMI, kg/m^2, mean (SD)	25.4 (3.2)	24.7 (3.3)	**<0.01**
Body weight, kg, mean (SD)	75.2 (11.6)	73.1 (11.6)	**<0.01**
Waist circumference, cm, mean (SD)	98.1 (10)	95.9 (9.8)	**<0.01**
Creatinine, umol/L	86.1 (22)	90.7 (23.4)	**0.04**
eGFR, ml/min, mean (SD)	79.4 (21)	75.2 (20.9)	**0.03**

Figure 1. Summary of the study results.

Domande “aperte”?



IMMUNE ACTIVATION / HYPERINFLAMMATION IN LESS DRUG REGIMENS: a (possible) new pharmacodynamic parameter

MONOTHERAPY (PI/r)

Merlini E, et al. *Antivir Ther.* (2018) 23:633–7.

Patients on monotherapy were more likely to display **increased T-cell apoptosis**

Torres B, et al. *J Int AIDS Soc.* (2014) 17:19246.

Patients on monotherapy display **higher levels** of monocyte activation—CD14+CD16-CD163+ cells and sCD14 levels.

Petrara MR, et al. *PLoS ONE.* (2017) 12:e0185128.

Significant increase of T- and B-cell activation in patients receiving one drug

DUAL THERAPY

Romero-Sánchez MC, et al. *Antiviral Res.* (2014) 111:26–32.

Belmonti S, et al. *J Antimicrob Chemother.* (2018) 73:1949–54.

Vallejo A, et al. *HIV Med.* (2019) 20:555–60.

No relevant changes in immune activation markers & a variety of soluble factors

Mussini C, et al. *BMC Med.* (2018) 16:79.

Higher CD8+ T-cell count in dual therapy

van Wyk J, et al. *J Acquir Immune Defic Syndr.* (2020) 85:325–30.

No consistent pattern of change from baseline to week 48 or differentiation between both groups in the following markers: IL-6, CRP, sCD14, sCD163, and D-dimer

van Wyk J, et al. Clinical Infectious Diseases 2020; , 71 (8): 1920–1929.

Significantly **smaller decrease** in serum IL-6 levels in patients on dual therapy, but for sCD14 there was an exact **opposite t**

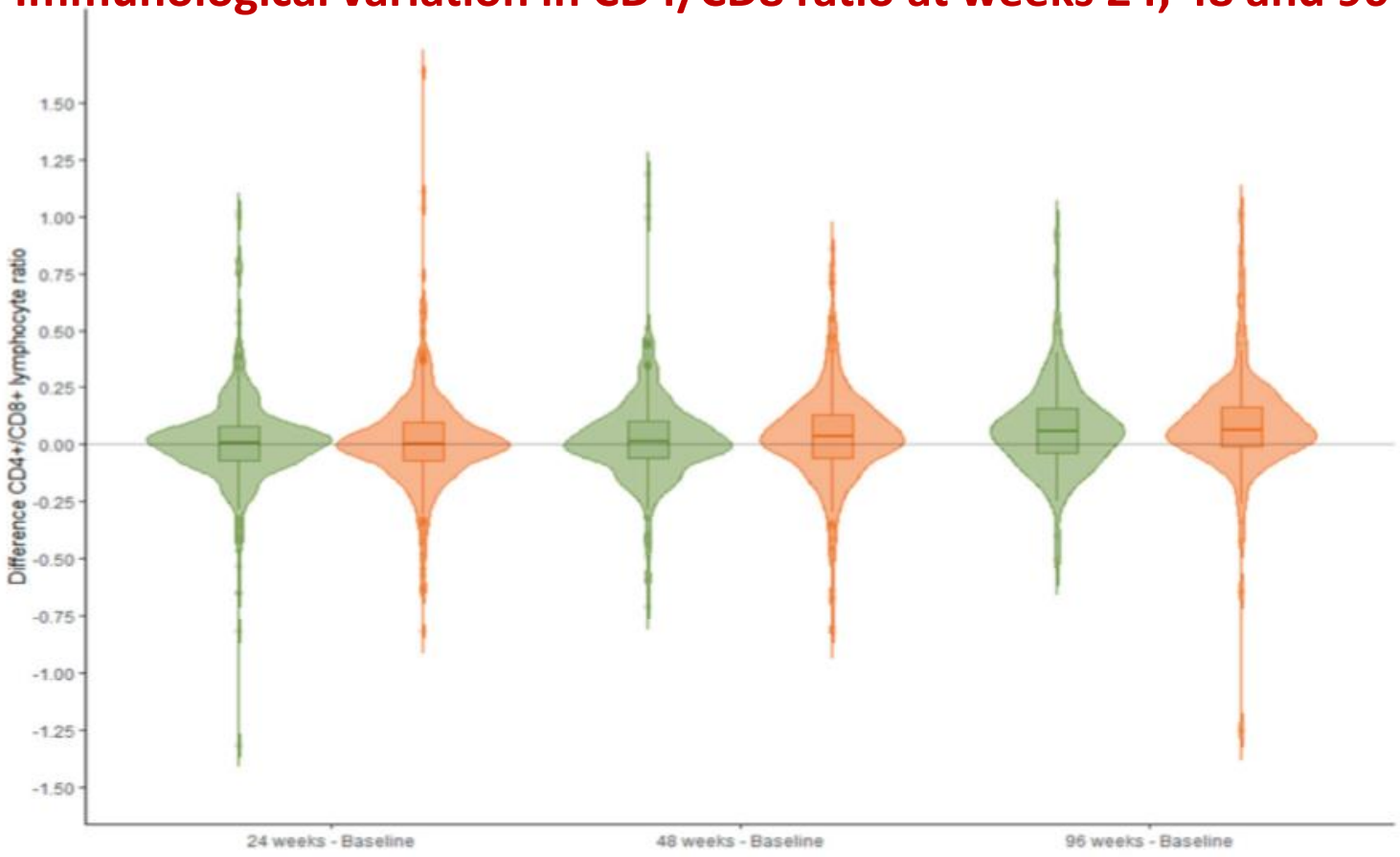
T-cell activation not tested

Article

Efficacy and Safety of Two-Drug Regimens with Dolutegravir plus Rilpivirine or Lamivudine in HIV-1 Virologically Suppressed People Living with HIV

Carlos Dueñas-Gutiérrez [1,*], Luis Buzón [2], Roberto Pedrero-Tomé [3], José A. Iribarren [4], Ignacio De los Santos [5], Sara De la Fuente [6], Guillermo Pousada [7], Miguel Angel Moran [8], Estela Moreno [9], Eva Ferreira [10], Julia Gómez [11] and Jesús Troya [12]

Immunological variation in CD4/CD8 ratio at weeks 24, 48 and 96



Viruses 2023, 15, 936

Serum biomarkers DTG/3TC vs. CAR

Trial	Week	Regimen	No.[a]	Visit to baseline ratio[b]					
				Blood D-dimer	Serum CRP	Serum IL-6	Serum sCD14	Serum sCD163	$CD4^+/CD8^+$ ratio[c]
SALSA	24 (20)	DTG/3TC	246		0.950	1.024	1.025	1.003	
		CAR	247		1.010	1.061	1.142	0.970	
	48 (20)	DTG/3TC	246		0.904	1.001	0.836	1.045	
		CAR	247		1.036	1.038	0.935	1.030	
							$P=.002$		
TANGO	48 (18)	DTG/3TC	369	0.968	1.012	0.990	0.953	0.916	0.95
		TAF-based regimen	371	0.995	1.083	0.852	0.982	0.904	0.96
						$P=.006$	$P=.048$		
	96 (22, 33)	DTG/3TC	369	0.956	0.889	1.112	1.041	0.822	0.985
		TAF-based regimen	371	0.932	0.945	1.040	1.090	0.806	1.040
	144 (33)	DTG/3TC	369	0.951	0.840	1.066	0.742	0.865	1.010
		TAF-based regimen	371	0.925	0.855	0.952	0.807	0.833	1.060
						$P=.039$	$P=.044$		

Improved Worsened

Llibre JM, et al. OFID 2022

Open Forum Infectious Diseases

MAJOR ARTICLE

Changes in Inflammatory and Atherogenesis Biomarkers With the 2-Drug Regimen Dolutegravir Plus Lamivudine in Antiretroviral Therapy–Experienced, Virologically Suppressed People With HIV-1: A Systematic Literature Review

Josep M. Llibre,[1] Pedro E. Cahn,[2] Janet Lo,[3] Tristan J. Barber,[4,5] Cristina Mussini,[6] Berend J. van Welzen,[7] Beatriz Hernandez,[8] Cynthia Donovan,[9] Michelle Kisare,[10] Myooran Sithamparanathan,[11] and Jean van Wyk[11]

[1]Infectious Diseases, Fundació Lluita contra la Sida, Hospital Universitari Germans Trias i Pujol, Barcelona, Spain, [2]Fundación Huésped, Buenos Aires, Argentina, [3]Metabolism Unit, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA, [4]Ian Charleson Day Centre, Royal Free London NHS Foundation Trust, London, United Kingdom, [5]Institute for Global Health, University College London, London, United Kingdom, [6]Clinic of Infectious Diseases, Azienda Ospedaliero-Universitaria Policlinico, and University of Modena and Reggio Emilia, Modena, Italy, [7]University Medical Centre Utrecht, Utrecht, The Netherlands, [8]ViiV Healthcare, Madrid, Spain, [9]ViiV Healthcare, Research Triangle Park, North Carolina, USA, [10]GlaxoSmithKline, Nairobi, Kenya, and [11]ViiV Healthcare, Brentford, United Kingdom

Background. The 2-drug regimen dolutegravir plus lamivudine has demonstrated long-term noninferior efficacy vs 3-/4-drug regimens (3/4DRs) in phase 3 trials. This systematic literature review summarizes clinical trial and real-world evidence evaluating impact of dolutegravir plus lamivudine on inflammatory and atherogenesis biomarkers in people with human immunodeficiency virus type 1 (PWH).

Methods. Using Ovid MEDLINE, Embase, PubMed, and Cochrane library databases and conference proceedings, we searched for studies published from 1 January 2013 to 14 July 2021, reporting changes in inflammatory and atherogenesis biomarkers with dolutegravir plus lamivudine in antiretroviral therapy–experienced, virologically suppressed PWH aged ≥18 years.

Results. Four records representing 2 randomized controlled trials (RCTs) and 6 records of real-world evidence met eligibility criteria. All real-world studies evaluated $CD4^+/CD8^+$ ratio, while only 1 assessed inflammatory biomarkers. Across both RCTs, no consistent pattern of change in biomarkers was observed between dolutegravir/lamivudine and 3/4DR comparators. There were significant changes in soluble CD14 favoring dolutegravir/lamivudine in TANGO at weeks 48 and 144 and SALSA at week 48, and in interleukin-6 favoring the control group in TANGO at weeks 48 and 144. In the real-world study evaluating inflammatory biomarkers, median soluble CD14 significantly decreased 48 weeks postswitch to dolutegravir plus lamivudine ($P < .001$), while other biomarkers remained stable. In all 6 real-world studies, increases in $CD4^+/CD8^+$ ratio were reported after switch to dolutegravir plus lamivudine (follow-up, 12–60 months).

Conclusions. Results show that dolutegravir plus lamivudine has a comparable impact on inflammatory and atherogenesis biomarkers vs 3/4DRs, with no consistent pattern of change after switch in virologically suppressed PWH.

Inflammatory Markers after Switching to a Dual Drug Regimen in HIV-Infected Subjects: A Two-Year Follow-Up

- Prospective single arm study of successfully treated subjects simplifying cART from triple to dual regimens.
- 14 subjects were included (mean age 60 years, 12 men, 26 years since HIV infection, CD4 nadir 302 cells/mm3, 18 years on cART, 53 months on last cART).
- sCD163 values increased significantly from baseline (+36%, p = 0.003) and from 6 months after the switch.

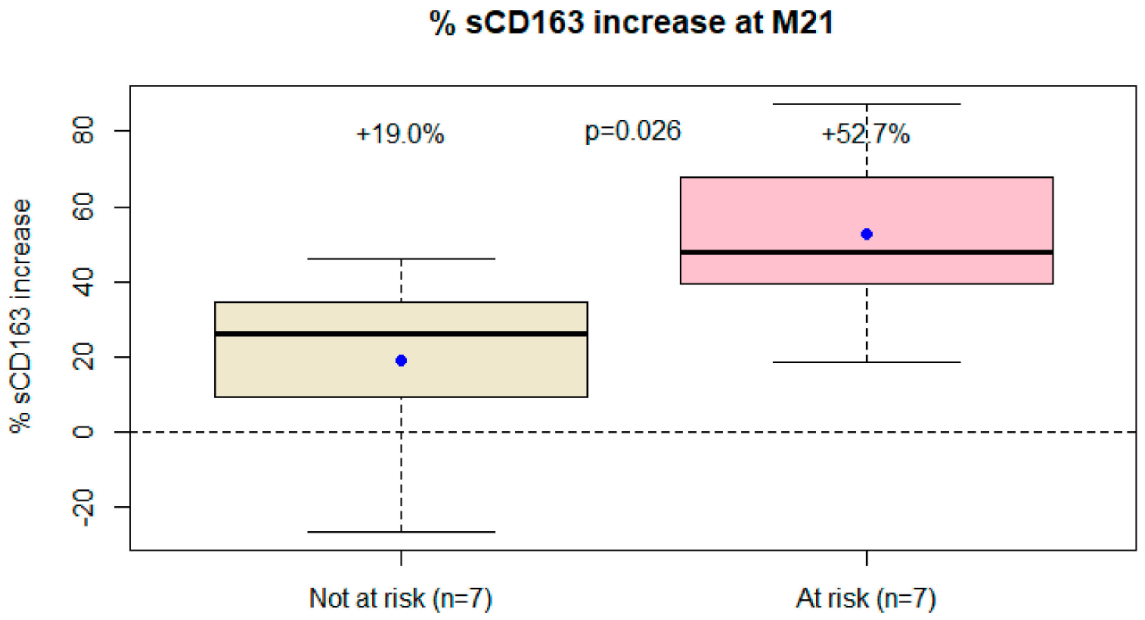
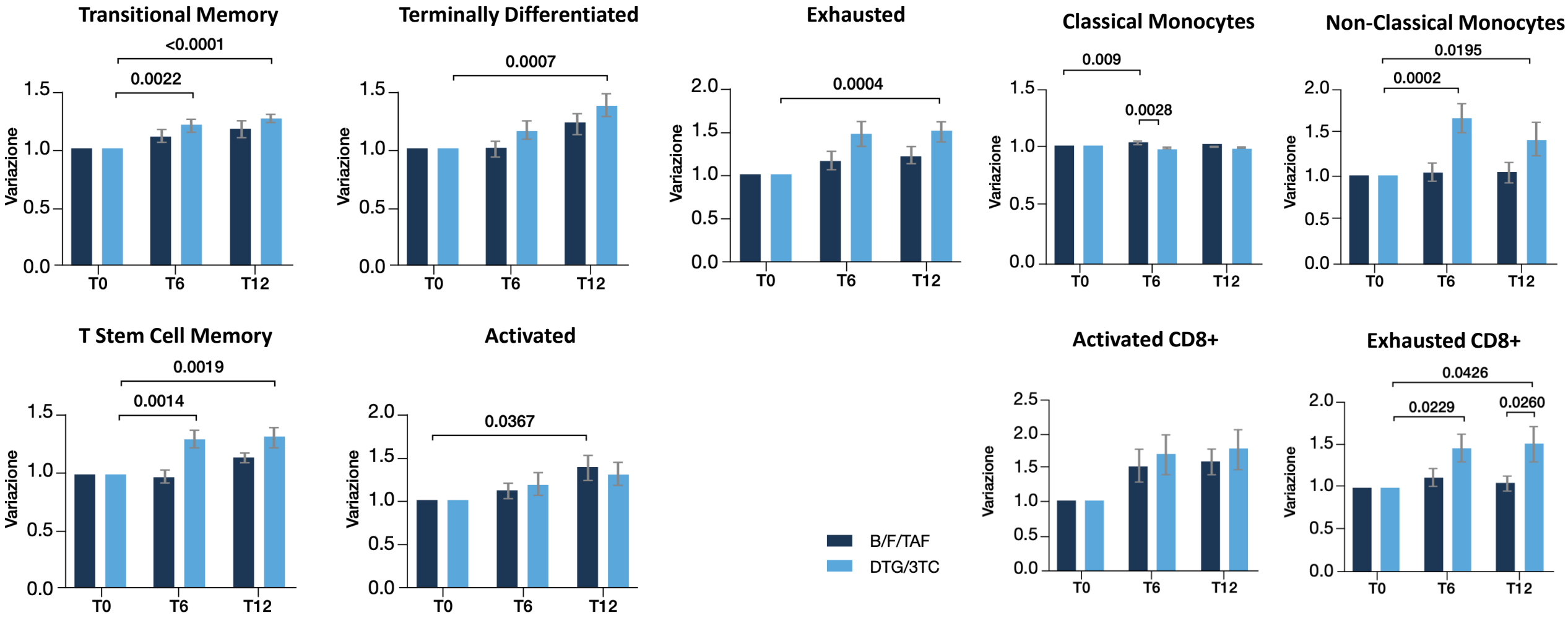


Figure 2. Differences in sCD163 trajectory from baseline to the end of follow-up between patients at risk of immune activation (i.e., CD4 nadir < 200 cc/mm^3, previous AIDS, or very low-level viremia during the follow-up) and those not at risk.

Vassallo M, et al. Viruses 2022

Changes in Immune Cells with 2DR

Open label, randomized, FTC/TAF/BIC vs. DTG/3TCn= 33 vs. 33

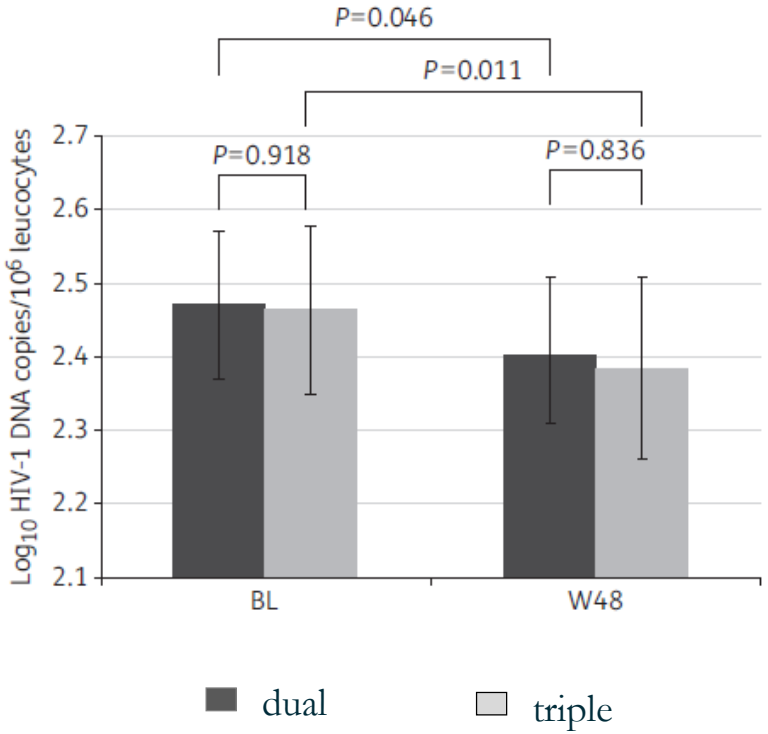


Cossarizza A et al. Glasgow 2022. P099

HIV DNA in 2DR options for HIV infection

ATLAS-M study
ATV/r + 3TC vs ATV/r+2NRTI

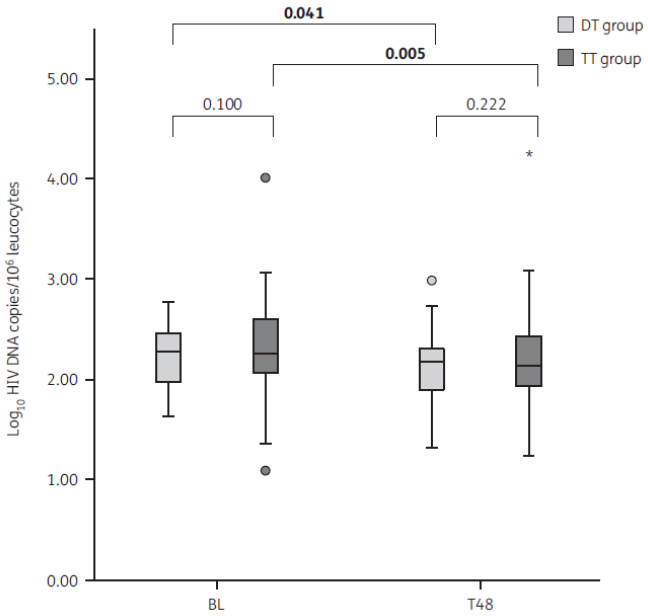
week 48



Lombardi F et al. JAC 2017;72:2055-2059.

Prospective, controlled study
DTG + 3TC (80 pts)

week 48



Lombardi F et al. JAC 2020.

ANRS 163 ETRAL study
ETR + RAL (single arm, 165 pts)

week 96

	HIV DNA change	
baseline	week 48	week 96
148 copies	+ 0	+ 0

Katlama C et al. JAC 2019.

Use of *Dovato* in Patients with M184V/I Resistance Mutation

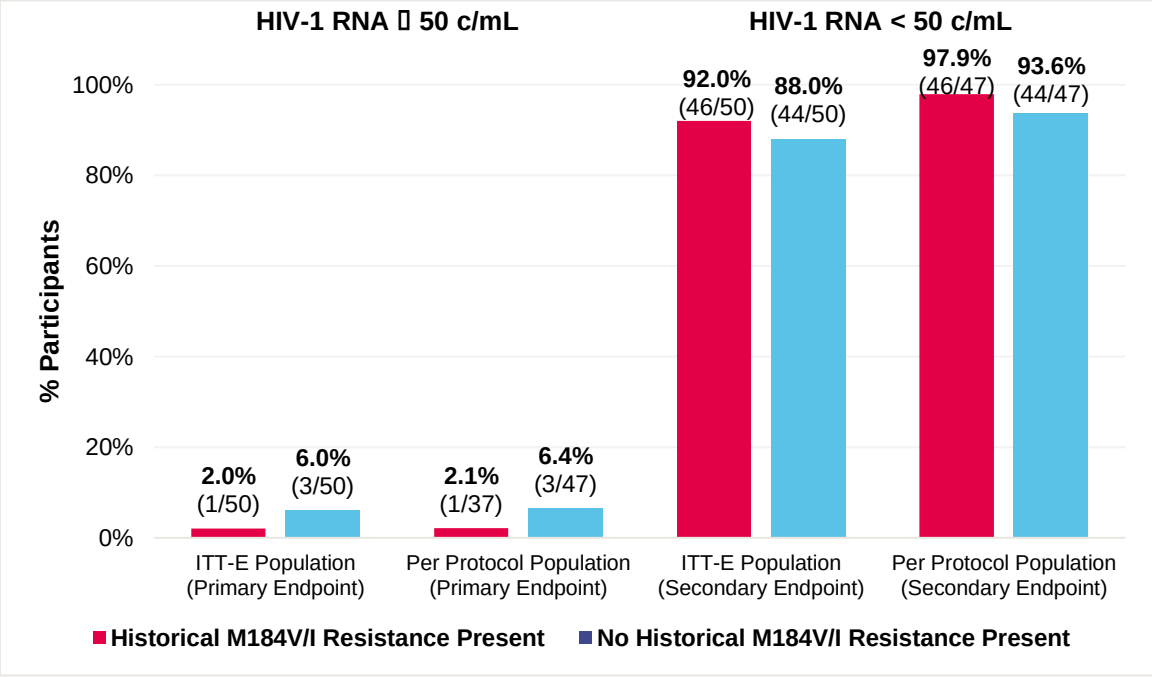
Summary

- *Dovato* (dolutegravir [DTG] + lamivudine [3TC]) is not recommended for use in patients with current or past history of resistance to any components of DTG/3TC.[1]
- In the TANGO and SALSA trial, 9 treatment-experienced participants with the M184V/I mutation (based on pro-viral DNA analysis) received DTG/3TC. All 9 patients maintained virological suppression (HIV-1 RNA < 50 copies/mL) at Week 48.[2,3]
- Limited prospective and observational cohort data are available specific to the use of DTG + 3TC in patients with varying levels of treatment experience and with a history of M184V/I.[4-16]
- There are no data available describing the use of DTG + 3TC in treatment naïve patients who have the M184V/I mutation at baseline.
- Important safety information and boxed warnings(s) can be found in the Prescribing Information link and can also be accessed at Our HIV Medicines.

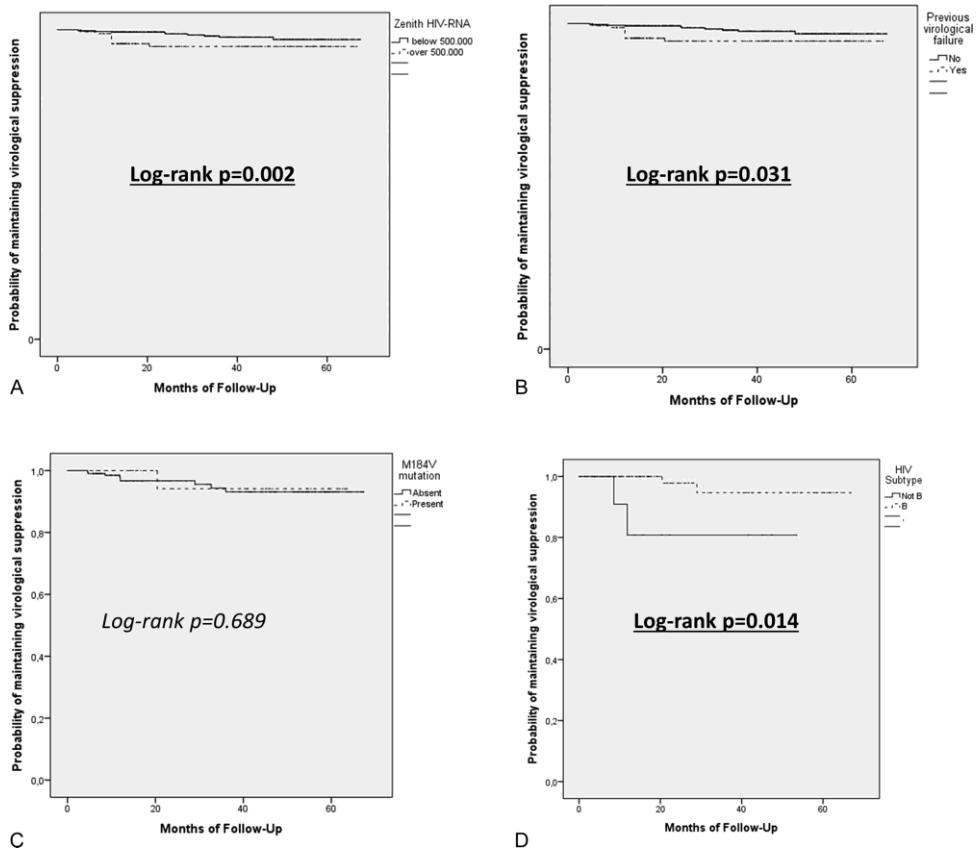
Data on patients switching to DTG + 3TC according to historical M184V

SOLAR 3D

Figure 1. Virologic Outcomes at Week 48 Based on Presence/Absence of Historical M184V/I[13]



785 pts: 96.4% VS at 5 years

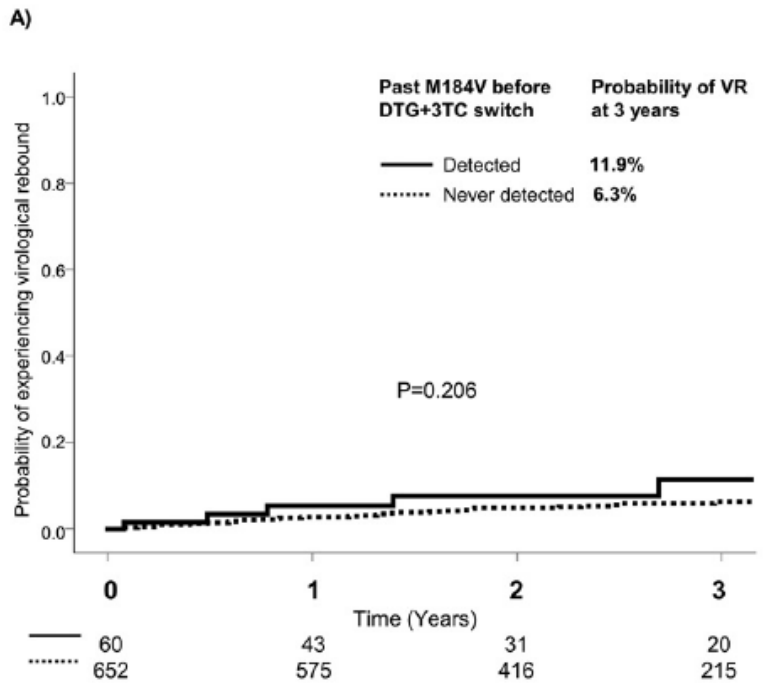


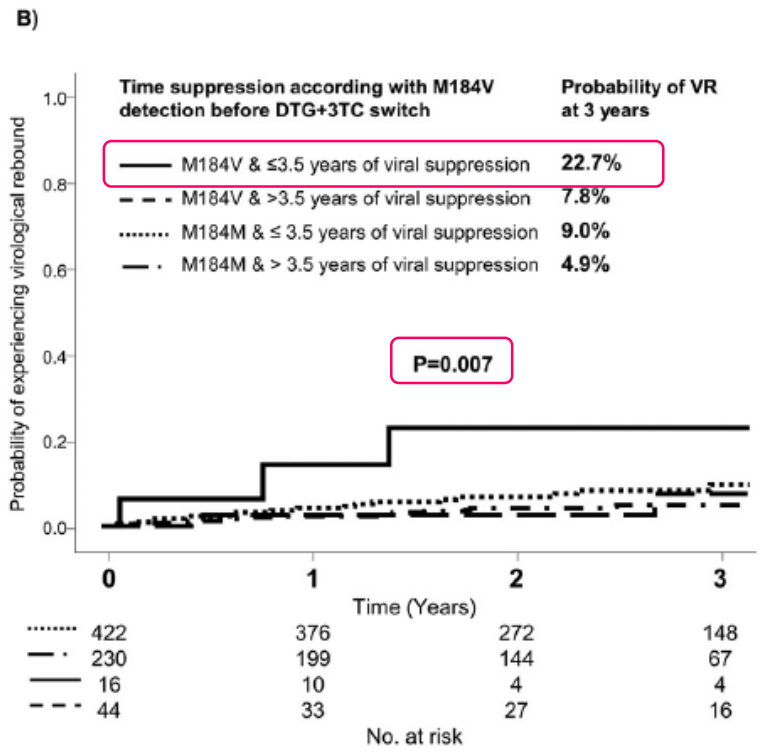
Blick G, et al. EACS 2021 PE2/65; Cicullo A, et al. JAIDS 2021

Virological efficacy of switch to DTG plus 3TC in a retrospective observational cohort of suppressed HIV-1 patients with or without past M184V: the LAMRES study

Maria Mercedes Santoro[a,1,*], Daniele Armenia[b,1], Elisa Teyssou[c], José Ramón Santos[d], Charlotte Charpentier[e], Sidonie Lambert-Niclot[f], Andrea Antinori[g], Christine Katlama[c], Diane Descamps[e], Carlo Federico Perno[h], Vincent Calvez[c], Roger Paredes[d], Francesca Ceccherini-Silberstein[a], Anne Geneviève Marcelin[c], for the LAMRES Study Group

- 712 individuals in France, Italy and Spain, 60 (8.4%) with past M184V
- By 3 years after switch, overall probability of VR and blips was 6.7% and 6.9%, without any statistical significance according to the presence/absence of past M184V.





Journal of Global Antimicrobial Resistance 31 (2022) 52–62

IAS 2023
23-26 July 2023
IAS 2023, the 12th IAS Conference on HIV Science

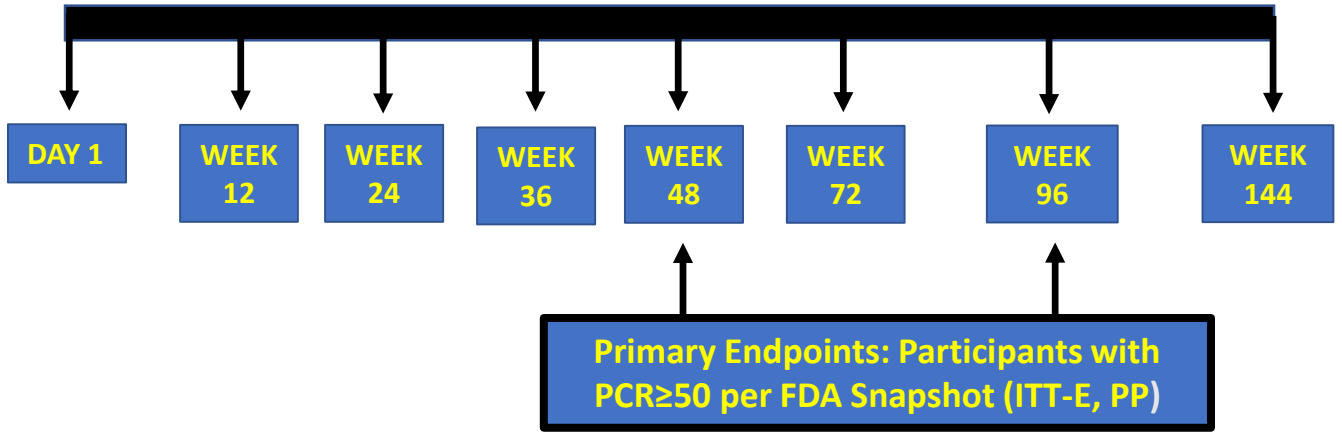
SOLAR-3D:
Prospective, open-label, comparative, 96-week study, [144-week extension] (n=100)

ELIGIBILITY CRITERIA:

- HIV+ Adults aged ≥18
- HIV-1 RNA <50c/mL for ≥6mos
- Any stable 2-/3-/4-drug ART for ≥6mos
- Prior virologic failure (≥2 prior ART with at least 1 of following: failure to attain PCR<50, confirmed rebound PCR>200, documented genotypic/ phenotypic resistance)
- No exclusion for prior INSTI, any CD4, prior NRTI mutations, or M184V/I or K65R in BL Proviral DNA NGS (above a 10% threshold)
- COVID Window +/- 1mo.

HISTORY OF PRIOR M184V/I (n=50)

NO HISTORY OF PRIOR M184V/I (n=50)



Individuals were consecutively consented and enrolled during regularly scheduled office appointments from 5/2/2019 through 6/16/20202

PRIMARY ENDPOINTS:

- Proportion of pts with PCR≥50 at Wks 48 & 96 (FDA Snapshot, ITT-E, Per Protocol)

SECONDARY ENDPOINTS:

- PCR<50 at Wks 48 & 96 (FDA Snapshot, ITT-E and Per Protocol)
- Discontinuations due to CVF (PCR≥50 followed by PCR≥200)

Blick et al. IAS 2023, #OAB0202

BASELINE CHARACTERISTICS

IAS 2023
23-26 July 2023
IAS 2023, the 12th IAS Conference on HIV Science

Baseline Characteristic	All Patients (n = 100)	Historical M184V/I Resistance (n = 50)	No Historical M184V/I Resistance (n = 50)	*P* Value
Median Age, yrs (IQR)	58 (51-64)	61 (56-66)	55 (47-61)	<0.001
Cis-/Trans-Gender Female, n (%)	15 (15)	11 (22)	4 (8)	0.050
Median Time Since HIV Diagnosis, yrs (IQR)	25.3 (15.0-29.5)	28.4 (25.1-30.0)	15.5 (9.8-26.7)	<0.001
Median CD4 Nadir cell/mm3 (IQR)	190 (64-278)	160 (45-225)	225 (88-359)	0.006
History CD4<200, n (%)	53 (53)	33 (66)	20 (40)	0.009
Median ART Duration, yrs(IQR)	22.3 (14.3-25.7)	24.6 (22.0-28.1)	15.2 (8.8-22.6)	<0.001
Median Previous ART regimens, n(IQR)	7 (4-10)	9 (7-13)	4 (2-5)	<0.001
Median Duration of HIV-RNA suppression, yrs (IQR)	11.8 (8.2-14.6)	12.8 (10.2-14.4)	8.9 (4.4-14.7)	0.019

There were no significant differences observed for Age at time of HIV diagnosis, Race, HBV/HCV, Median highest PCR or History PCR>100,000c/mL

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SWITCH CHARACTERISTICS

IAS 2023
23-26 July 2023
IAS 2023, the 12th IAS Conference on HIV Science

Switch Characteristic	All Patients (N = 100)	Historical M184V/I Resistance (n = 50)	No Historical M184V/I Resistance (n = 50)	*P* Value
On 3TC/FTC, n (%)	73 (73)	34 (68)	39 (78)	0.260
Median Time on DTG/3TC, weeks (IQR)	137.8 (133-151)	137.4 (133-151)	138.3 (132-151	0.747
CD4 at Switch, Median (IQR)				
• CD4%	30 (25-39)	27 (24-37)	32 (27-39)	0.136
• CD4 abs count, cells/mm#	610 (425-781)	617 (412-758)	593 (434-812)	0.677
• CD4<200, n (%)	1 (1)	1 (2)	0	0.315
• CD4<350, n (%)	10 (10)	7 (14)	3 (6)	0.182
PCR at Switch, Median (IQR)				
• Copies/mL	1 (1-19)	1 (1-19)	1 (1-19)	0.335
• Log_{10}	0 (0-1.3)	0 (0-1.3)	0 (0-1.3)	0.806
• PCR>50, n (%)	2 (2)	1 (2)[§]	1(2)[†]	1.000
• PCR, TND, n (%)	58 (58)	28 (56)	30 (60)	0.685

[§]1 pt with a screening PCR<50 was PCR 73 c/mL at BL; [†]1 pt with screening PCR<50 was PCR 4150 c/mL at BL

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BASELINE ART AND PROVIRAL MUTATIONS

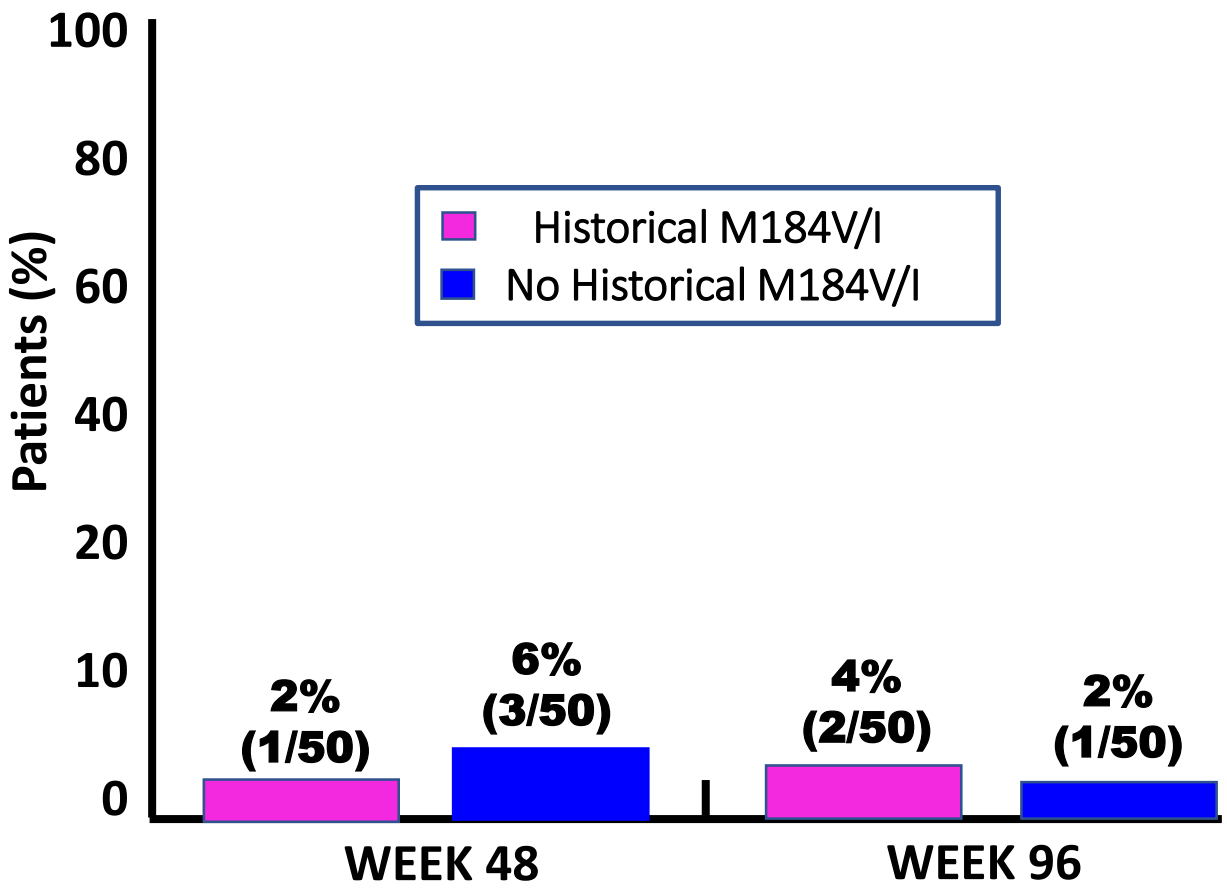
IAS 2023
23-26 July 2023
IAS 2023, the 12th IAS Conference on HIV Science

Baseline ART	All Patients (n=100)	Historical M184V/I (n=50)	No Historical M184V/I (n=50)
ART Regimen, n (%):			
• 2 NRTIs + INSTI: ❖ **TAF/FTC/BTG** ❖ **ABC/3TC/DTG** ❖ **TDF or TAF/FTC + DTG**	58 (58) **4 (4)** **51 (51)** **3 (3)**	30 (60) **3 (6)** **26 (52)** **1 (2)**	28 (56) **1 (2)** **25 (50)** **2 (4)**
• 2DR (NNRTI + INSTI): ❖ **RPV/DTG**	21 (21)	12 (24)	9 (18)
• 2 NRTIs + boosted INSTI: ❖ **TAF/FTC/EVG/c**	6 (6)	0	6 (12)
Historical GT vs Proviral DNA NGS			
M184V/I on Historical GT, n (%):	**50 (50)**	**50 (100)**	**0**
Proviral DNA by NGS, n (%): • M184V/I present • M184V/I absent • **K65R present** • **K65R present with Q151M**	**70 (70)** **15 (21)** **55 (79)** **1 (1)** **1 (1)**	41 (82) 15 (37) 26 (63) **1 (2)** **0**	29 (58) **0** **29 (100)** **0** **1**

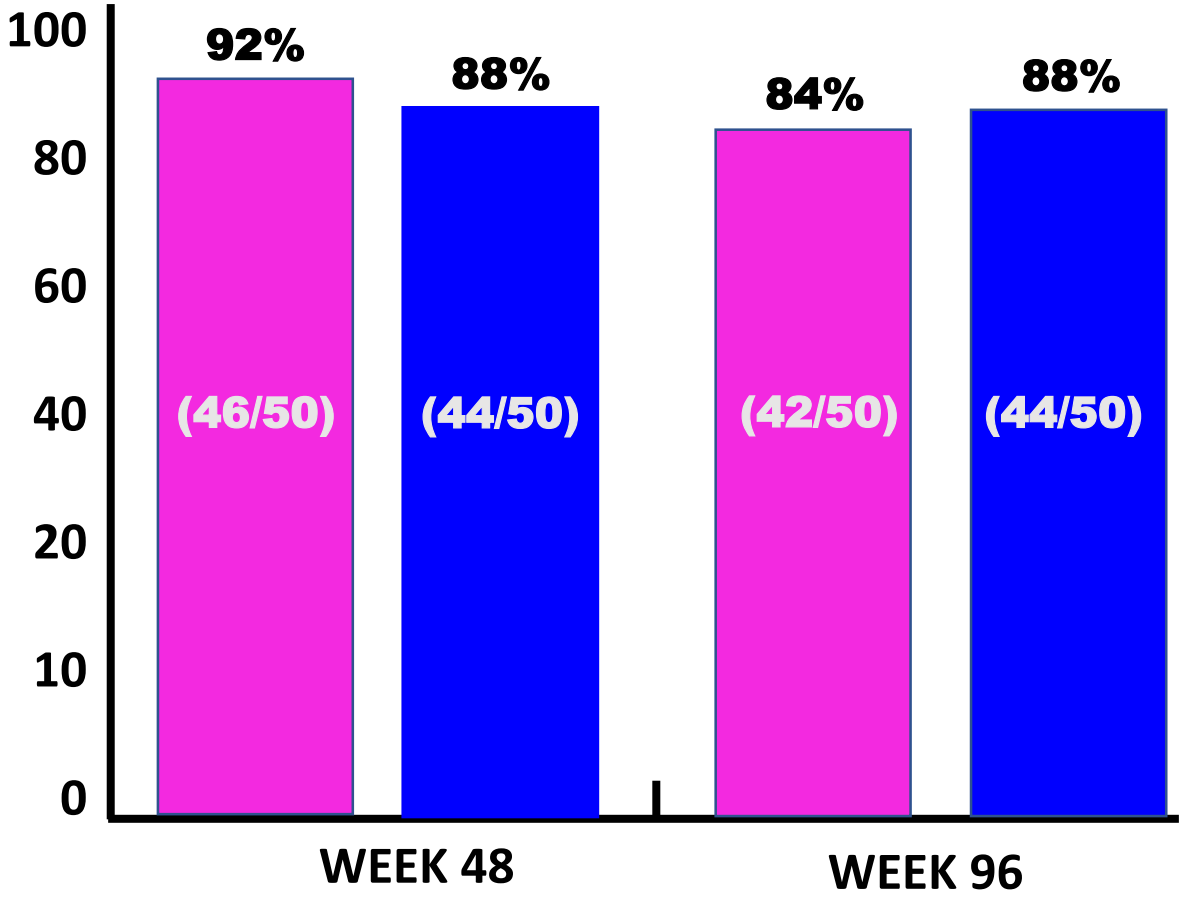
NGS = Next-Generation Sequence; Performed by Quest Diagnostics; Resistance-associated mutations present in 10% or more of viral species sequenced are reported

Blick et al. IAS 2023, #OAB0202

VIROLOGIC OUTCOMES:
Primary & Secondary Endpoints, Wks 48 & 96, ITT-E



PRIMARY ENDPOINT
PCR ≥ 50 c/mL by FDA Snapshot



SECONDARY ENDPOINT
PCR < 50 c/mL by FDA Snapshot

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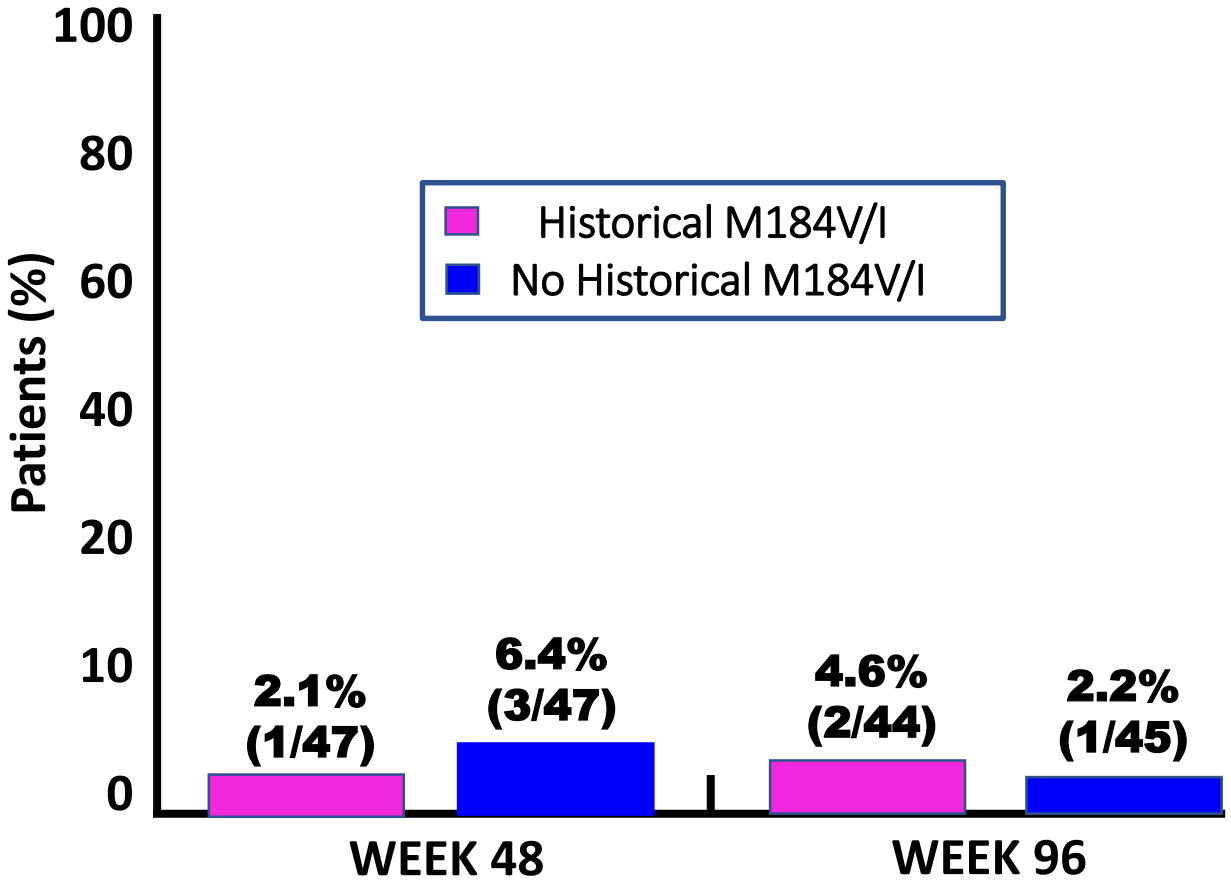
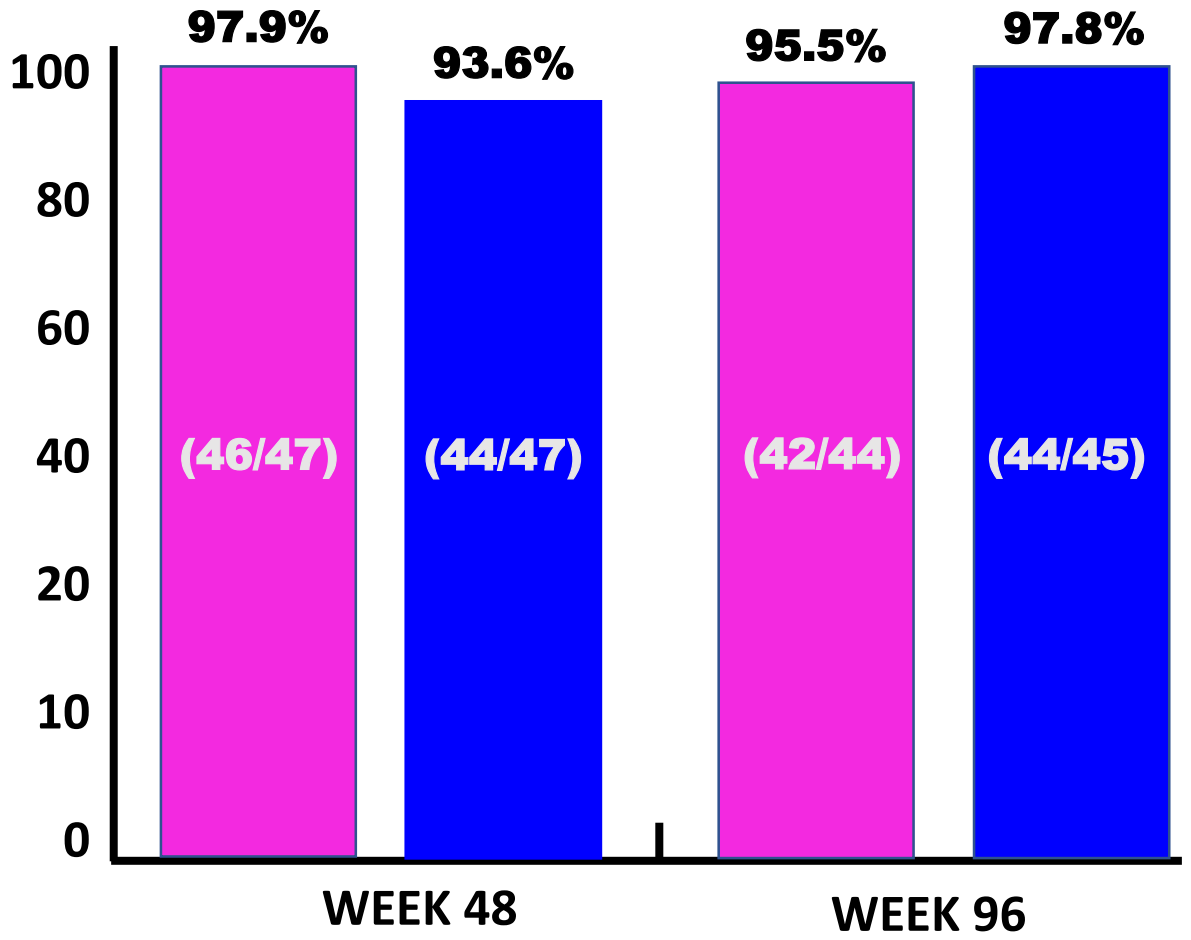
VIROLOGIC OUTCOMES:
Primary & Secondary Endpoints, Wks 48 & 96, Per Protocol



PRIMARY ENDPOINT
PCR ≥ 50 c/mL by FDA Snapshot



SECONDARY ENDPOINT
PCR < 50 c/mL by FDA Snapshot

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VIROLOGIC DISPOSITIONS: Week 96, ITT-E Population

N (%)	Historical M184V/I (n=50)	No Historical M184V/I (n=50)
PCR<50 c/mL	42 (84)	44 (88)
PCR≥50 c/mL	2 (4)	1 (2)
Data in window but PCR≥50 c/mL	2 (4)	1 (2)
• Resuppressed PCR<50 c/mL on F/U	2	1
Discontinued for lack of efficacy	0	0
NO VIROLOGIC DATA	6 (12)	5 (10)
Outside Week 96 window	0	1 (2)
Discontinued because of Drug-Related AE	1 (2)	0
Discontinued due to Death	3 (6)§	**2 (4)†**
LTFU	1 (2)	**1 (2)**
Incarcerated	1 (2)	**1 (2)**

§3 deaths unrelated to study drug: 1 prior to Week 36 due to probable cardiac arrhythmia from pre-existing cardiomyopathy, 1 prior to Week 48 from cardiorespiratory arrest, 1 after week 48 from hemorrhagic stroke; †2 deaths unrelated to study drug: 1 prior to Week 48 from suicide, 1 after week 72 died in sleep at home/? suicide

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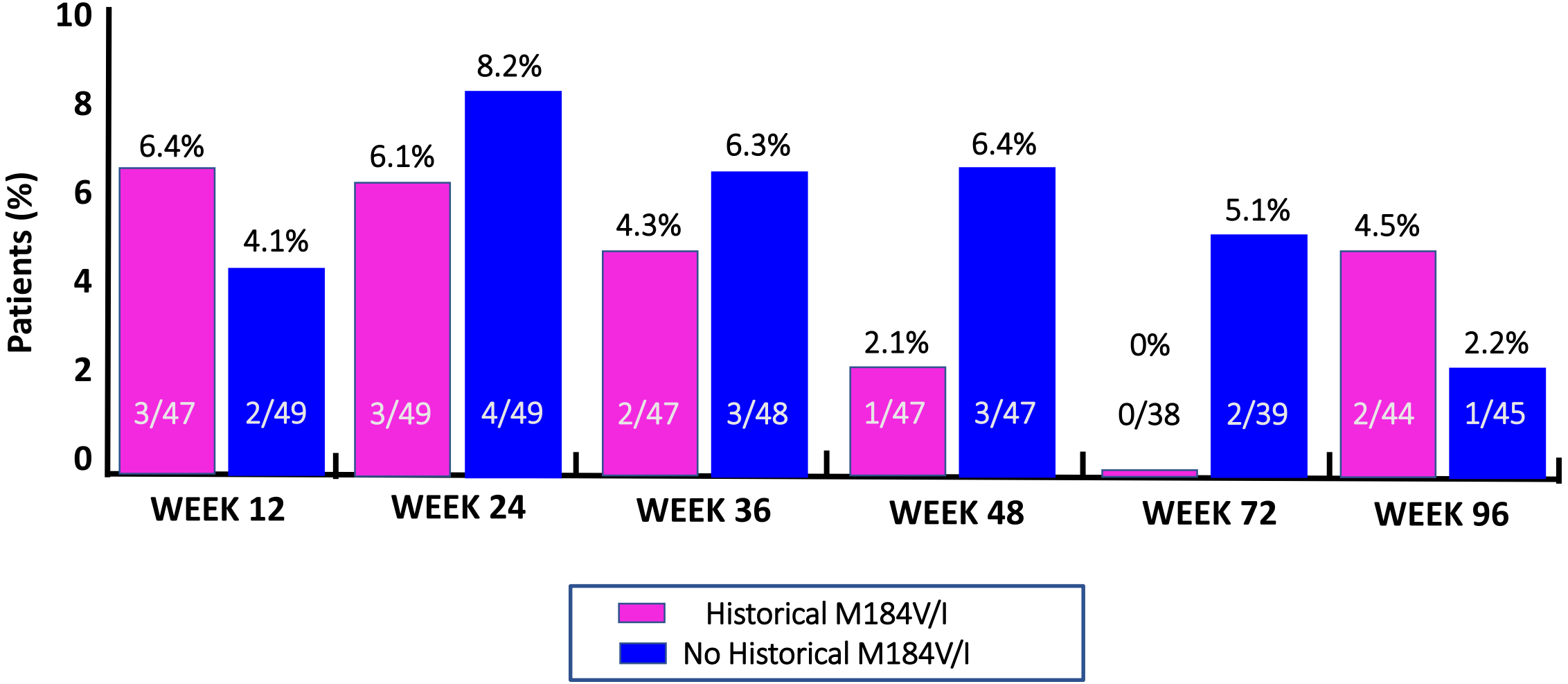
VIRAL LOAD “Blips”: Through Week 96

IAS 2023
23-26 July 2023
IAS 2023, the 12th IAS Conference on HIV Science

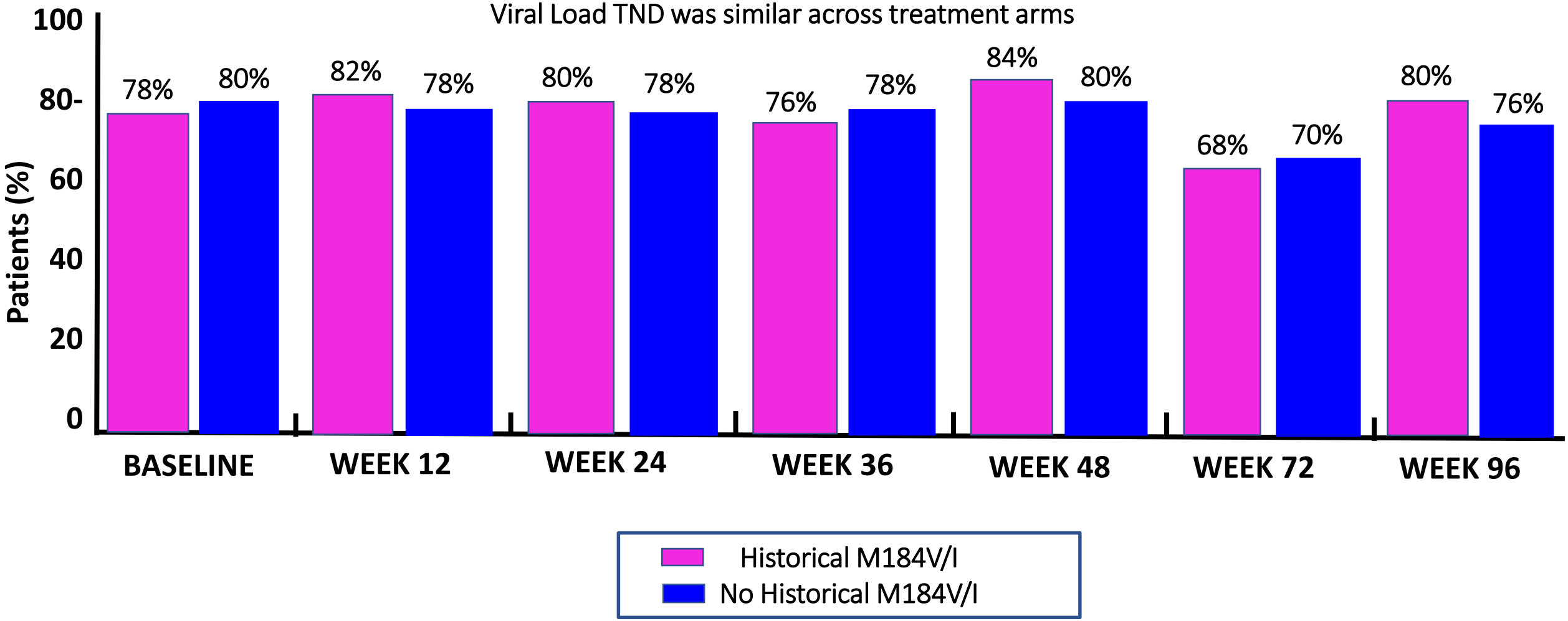
A viral load “blip” was defined as a viral load of 50 to <200 c/mL that resuppressed with adjacent PCR <50 c/mL
The occurrences of “blips” by visit were similar across treatment arms; HIV-1 RNA resuppressed in all patients



VIRAL LOAD Target Not Detected (TND): Through Week 96

IAS 2023
23-26 July 2023
IAS 2023, the 12th IAS Conference on HIV Science

Viral Load TND was defined as a VL <20c/mL
Viral Load TND was similar across treatment arms



2-drug regimens and HIV control into CNS

No Changes in Human Immunodeficiency Virus (HIV) Suppression and Inflammatory Markers in Cerebrospinal Fluid in Patients Randomly Switched to Dolutegravir plus Lamivudine (Spanish HIV/AIDS Research Network, PreEC/RIS 62)

Tiraboschi JM et al. JID 2020

Dual antiretroviral therapies are effective and safe regimens in the central nervous system of neurologically symptomatic people living with HIV

Trunfio M et al. AIDS 2020

Efficacy, pharmacokinetics and neurocognitive performance of dual, NRTI-sparing antiretroviral therapy in acute HIV-infection

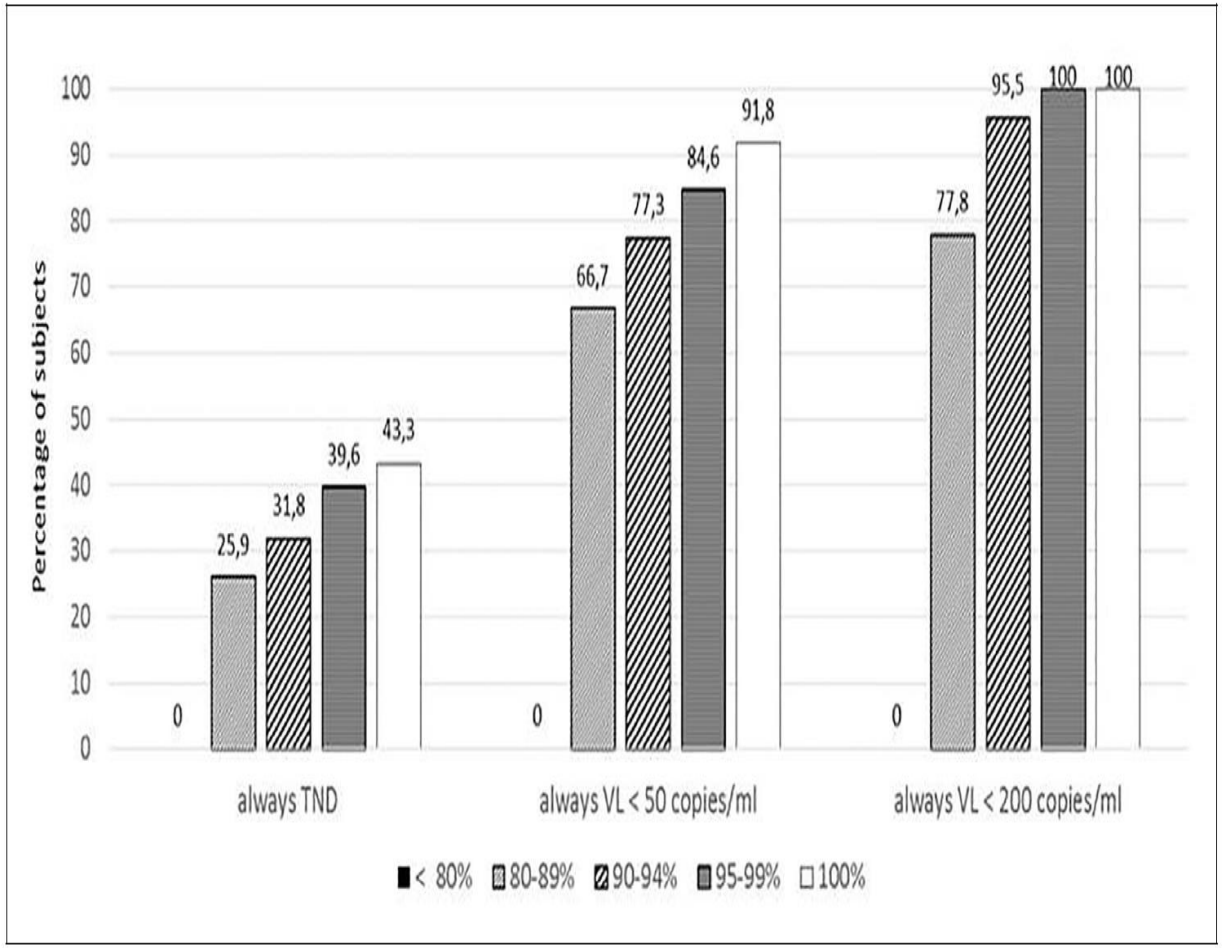
Gay CL et al. AIDS 2020

Efficacy and safety of two-drug regimens for treatment of HIV in the central nervous system

Gabuzda D et al. AIDS 2020

Forgiveness of DTG/3TC

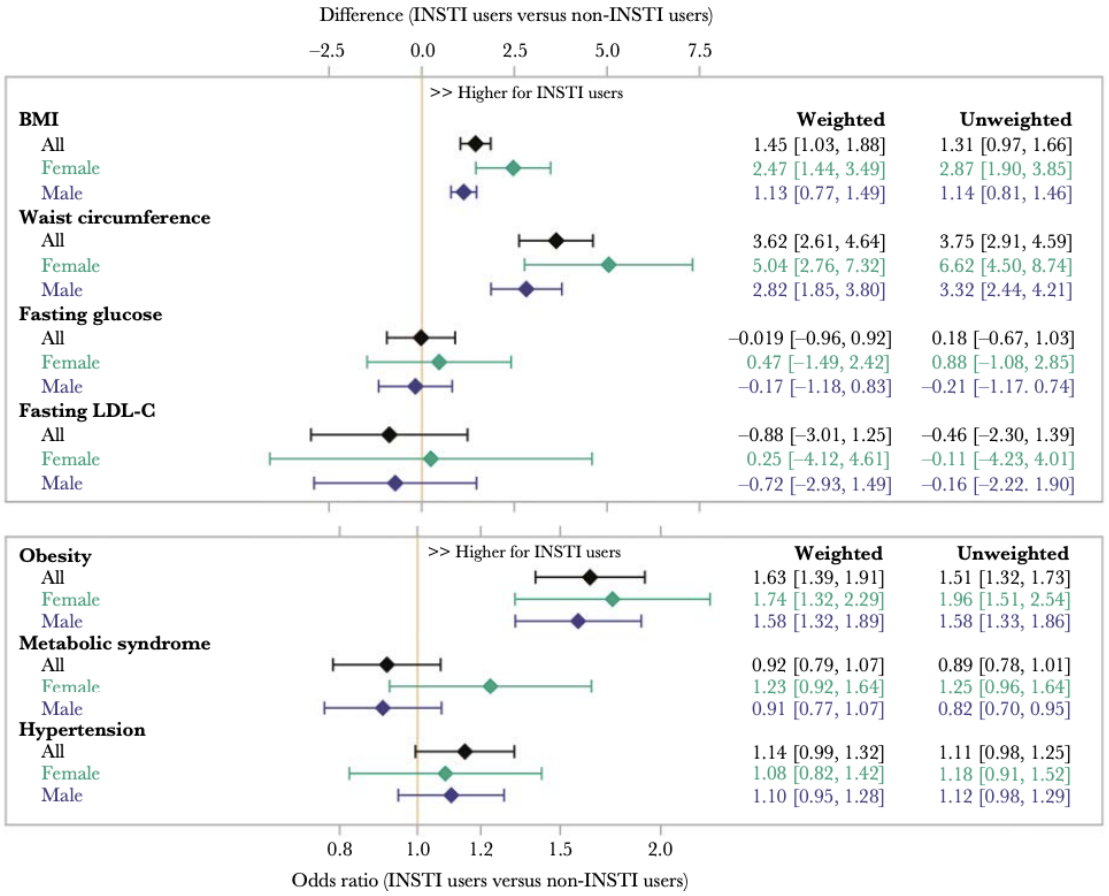
- 240 pts treated with 3TC/DTG
- Adherence measure: PDC = proportion of days covered
- Median FU 819 d (IQR 450-1459), 681 PYFU
- Median adherence 99% (IQR 95-100%)
- 10 non responders, 29 pts with non confirmed blips
- Slightly worse forgiveness compensated with overall high adherence

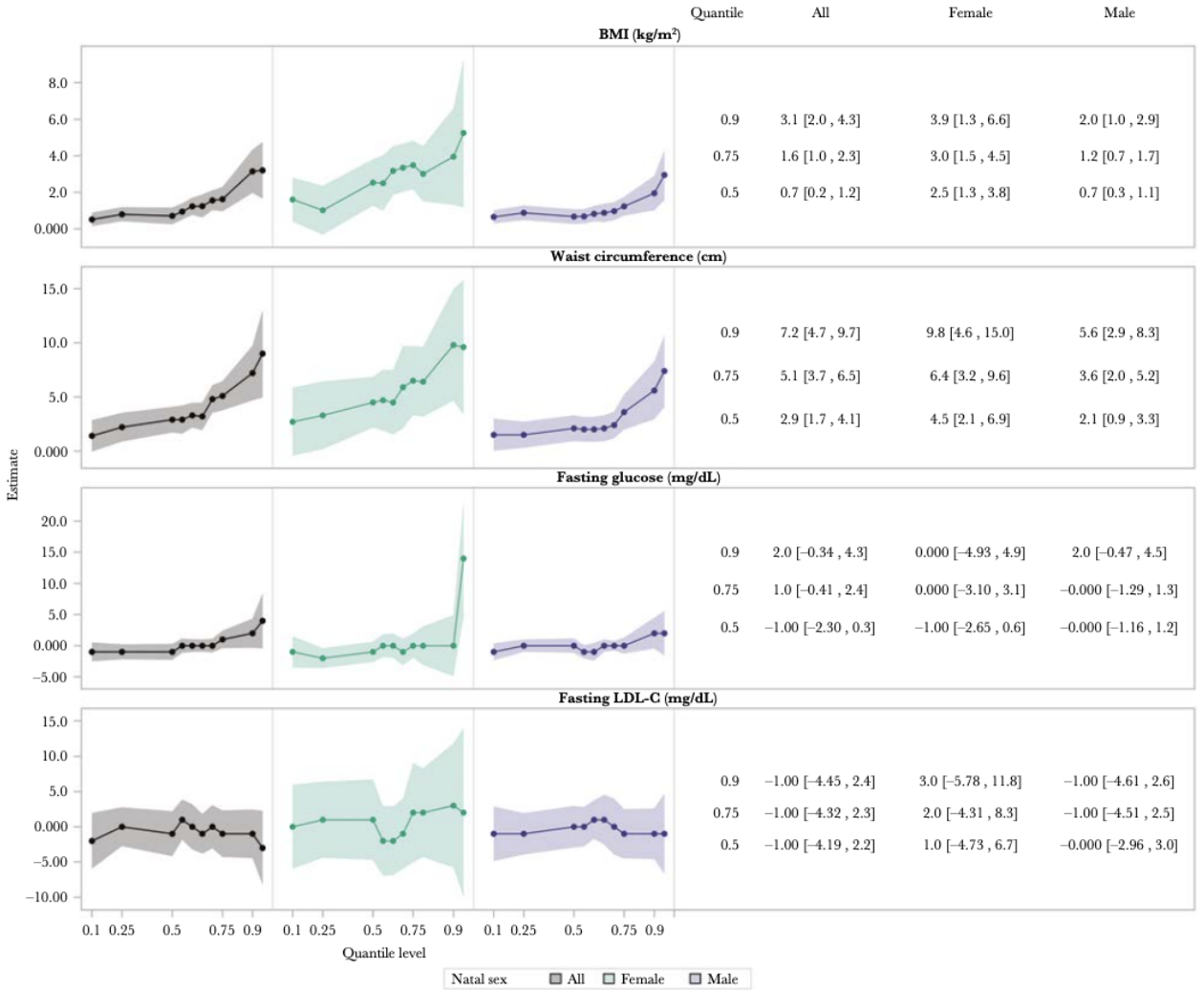


Maggiolo F, et al., J Int Assoc of Providers of AIDS Care, 2022

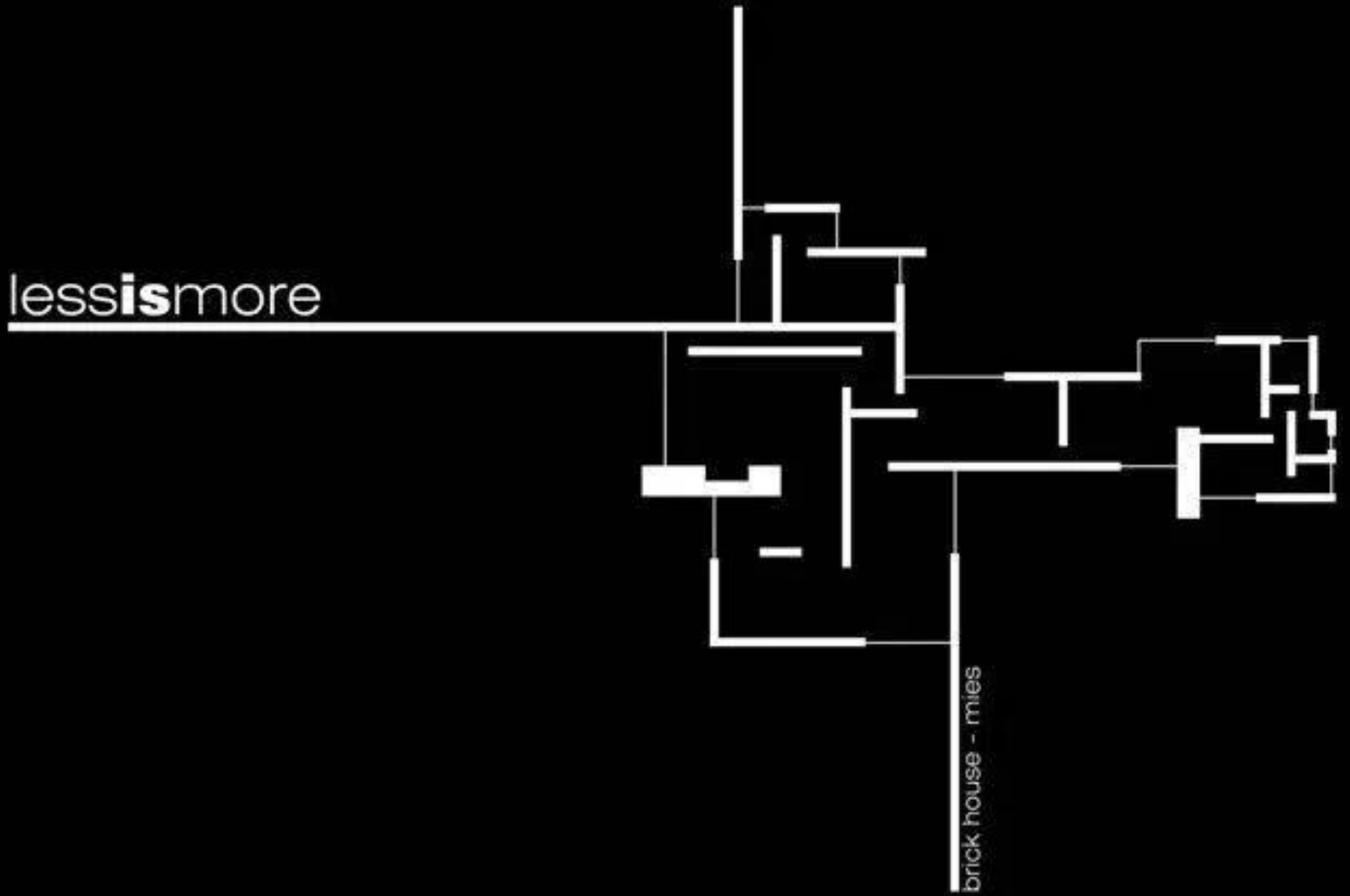
4500 REPRIEVE patients

Kileel EM, et al. OFID 2022





lessismore



CONCLUSIONI

- I dati a favore di una semplificazione a DTG/3TC in pazienti con soppressione virologica sono molto favorevoli e dimostrano efficacia prolungata in assenza di evidienti effetti avversi
  - L'impatto di una pregressa M184V e della durata della SV sono ancora in discussione
  - Aderenza parametro essenziale ma di difficile valutazione
  - Disturbi neurocognitivi?
  - Impatto metabolico degli INSTIs?
- DTG/RPV ha dati similmente favorevoli ma pochi fallimenti con selezione di RAMs sono stati osservati
- Le altre Dual hanno indicazioni limitate (PI+3TC) o dati ancora parziali e osservazionali (DTG+DOR o DOR+3TC)

Grazie per
l’attenzione